DEVOTED TO RESEARCH AND CLINICAL STUDY OF THE DISEASES AND PROCESSES OF AGING

Geriatrics

VOLUME 8 • NUMBER 11 November 1953

in peripheral vascular disorders

for

more

blood

flow . . . **Priscoline®**

hydrochloride

(tolazoline hydrochloride Ciba)

orally and

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effective

Average rise in skin temperature of toes in 15 patients after a single intravenous injection of Priscoline. (Reedy, W. J.: J. Lab. & Clin. Med. 37:365, 1951.)

Of the peripheral vasodilating agents available "Priscoline, given orally in doses of 0.025 to 0.050 Gm. every three or four hours, appears to be the most practicable for prolonged clinical trial." (Cecil and Loeb: Textbook of Medicine, ed. 8, 1951, p. 1189.)

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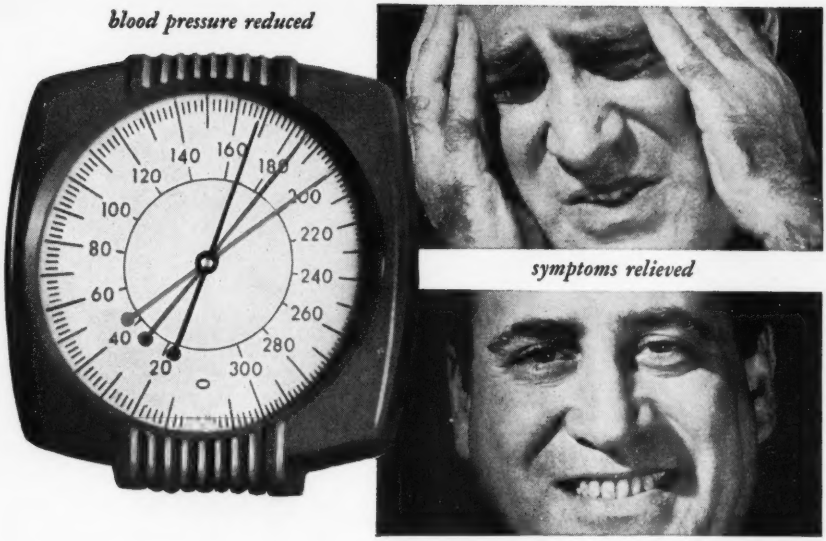

A drug of choice for long term oral treatment of hypertension . . . *found effective in 81% of patients*[1]

Lower blood pressure has been obtained in 81% of moderate and severe hypertensives treated with hexamethonium chloride (available as Methium) under general-practice conditions.[1] In 60% of these patients lower pressures continued for 4 to 16 months of the study.

Also, as pressure is reduced, improvement is almost universally seen in eye and heart symptoms, headache, vertigo, dyspnea, etc.[1-6] In some cases even where pressure fails to respond, symptoms may nonetheless abate.[4-7]

Methium, a potent autonomic ganglionic blocking agent, reduces blood pressure by interrupting nerve impulses responsible for vasoconstriction. Because of its potency, careful use is required. Pre-treatment patient-evaluation should be thorough. Special care is needed in impaired renal function, coronary artery disease and existing or threatened cerebral vascular accidents. *A booklet of complete instructions for prescribing is available and should be consulted prior to initiating therapy.*

1. Moyer, J. H., et al.: Am. J. M. Sc. *225*:379 (April) 1953.
2. Mills, L. C., and Moyer, J. H.: A.M.A. Arch. Int. Med. *90*:587 (Nov.) 1952.
3. Frankel, E.: Lancet *1*:408 (Feb. 17) 1951.
4. Johnson, I., et al.: Texas State J. M. *48*:331 (June) 1952.
5. Council on Pharmacy and Chemistry: J.A.M.A. *151*:385 (Jan. 31) 1953.
6. Grimson, K. S., et al.: J.A.M.A. *149*:215 (May 17) 1952.
7. Turner, R.: Lancet *1*:1217 (June 2) 1951.

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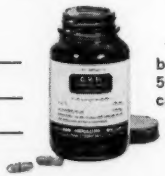

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Thiamine hydrochloride	10 mg.
Riboflavin	10 mg.
Niacinamide	100 mg.
Calcium pantothenate	40 mg.
Pyridoxine hydrochloride	5 mg.
Choline bitartrate	500 mg.
Folic acid	2.5 mg.
Vitamin B_{12} (crystalline)	4 mcg
Iron	15 mg.
Calcium	6.3 Gm.
Phosphorus	4.5 Gm.
Sodium	1.9 Gm.
Potassium	7 Gm.

Sustagen contains powdered whole milk, non-fat milk solids, calcium caseinate and Dextri-Maltose plus vitamins and iron.

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For detailed information, write for the booklet "How to Use Sustagen."

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GERIATRICS

November, 1953
Volume 8
Number 11

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GERIATRICS is published monthly at 84 South Tenth Street, Minneapolis 3, Minnesota by Lancet Publications, Incorporated. Subscription rates: $8.00 a year, 75c a copy; foreign, $9.00 a year, 85c a copy. Entered as second class matter February 14, 1946, at the post office at Minneapolis, Minnesota, under the act of March 3, 1879.

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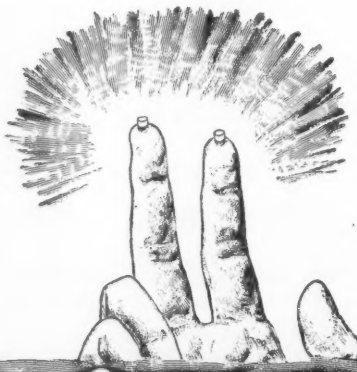

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Looking forward

Papers and authors you will meet in the December issue . . .

Preoperative Preparation of the Aged Patient Facing Emergency Surgery may mean the difference between success or failure on the operating table, according to Sidney E. Ziffren, M. D., associate professor of surgery, and Raymond F. Sheets, M. D., assistant professor of medicine at the University of Iowa College of Medicine. Because of the physiologic limits imposed by age, compromise measures are sometimes necessary in preoperative management. Blood volume must be watched, whole blood administered when necessary, and constant attention given to signs of shock and congestive heart failure.

•

Headaches with arteriosclerotic or essential hypertension were partially or completely relieved with sublingual administration of CCK 179 in 86 per cent of 42 patients studied by Travis Winsor, M. D., assistant clinical professor of medicine at the University of Southern California Medical School. In his studies on the **Effect of Hydrogenated Alkaloids of Ergot on Hypertensive Headaches,** Dr. Winsor found that the agent was also effective in the prophylaxis of migraine in a large percentage of a small series of patients.

•

Physical treatment, like drug therapy, is the physician's responsibility, writes Harold Dinken, M. D., in **Physical Medicine in the Treatment and Rehabilitation of Rheumatic Disease.** The practitioner must not only prescribe such treatment intelligently, but be responsible for seeing that it is carried out.

Dr. Dinken, who is head of the Department of Physical Medicine and Rehabilitation at the University of Colorado School of Medicine at Denver, evaluates various forms of treatment for rheumatic disease—thermotherapy, mechanotherapy, therapeutic exercises and rehabilitation, including social, educational and vocational retraining. He discusses the pathology, symptomatology and physical treatment of periarticular rheumatic disease.

•

The lipotropic activity of a new synergistic combination, Lipotaine, consisting of betaine, choline, liver extract and vitamin B_{12}, was studied for one year in a series of 102 patients by Lester M. Morrison, M. D., senior attending physician and chief of medical service at Los Angeles County General Hospital. Writing on **The Therapeutic Action of Betaine-Lipotropic Combinations in Clinical Practice,** he reports that in Group A, consisting of 40 patients with proven coronary atherosclerosis treated with Lipotaine compared with 40 similar patients who were untreated, there were no deaths in the treated series, and 10 cardiac deaths in the control group. He also found that serum cholesterol levels were effectively reduced and serum phospholipid levels effectively elevated.

•

For these and other articles, abstracts, reviews and special features, read every issue of Geriatrics.

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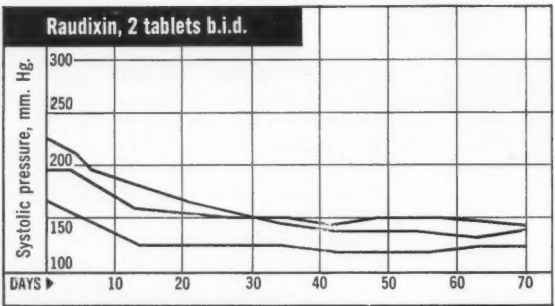
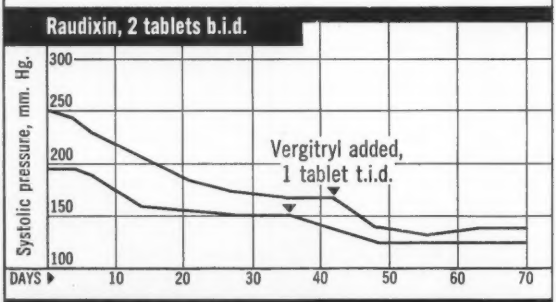


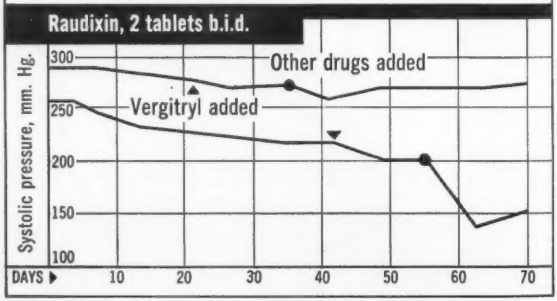
step 2

If blood pressure is not adequately controlled in four to eight weeks, Vergitryl (veratrum) may be added to Raudixin. This brings many of the remaining patients under control. Raudixin tends to delay tolerance to Veratrum, and makes smaller dosage possible.



step 3

For the few patients resistant to this combined regimen, a more potent drug may be added, for example, Bistrium (hexamethonium). The most potent drugs, which are potentially dangerous, are thus used only as a last resort in the most refractory cases.



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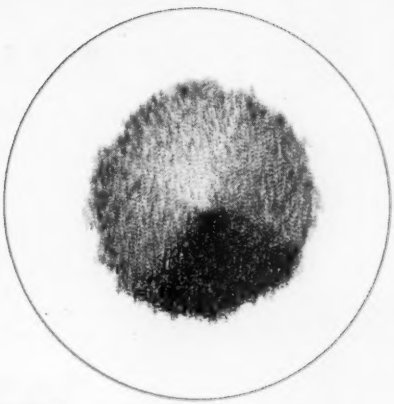

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supplied: 4-ounce and 16-ounce packages.

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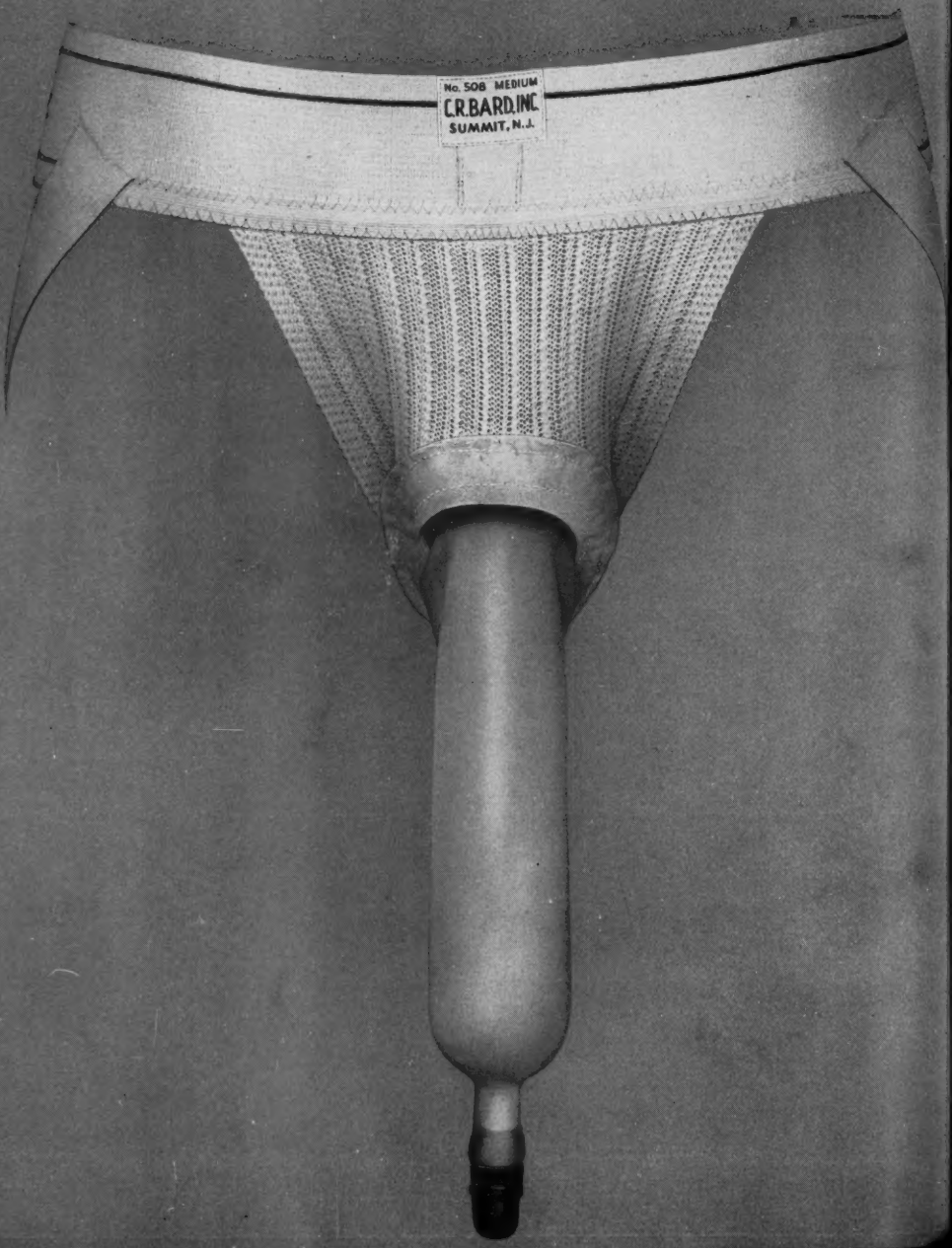
The New McGuire Urinal . .



Weighs Less Than 3 Ounces

ELASTIC BELT FITS COMFORTABLY AND SPECIAL FEATURE AVOIDS LEAKAGE

The new McGuire Urinal is unusually light because the bag is of latex and is attached to the pouch of an "athletic" supporter. The elastic belt and leg straps fit comfortably with no belts or buckles to adjust.

One outstanding feature is the conical-shaped, penile sheath permanently attached inside the bag. It can be cut with a pair of scissors to the proper size for perfect fit and comfort. There is never any danger of leakage, even when the patient is sitting or lying down.

One report says that this new McGuire Urinal "has been most satisfactory in the care of paraplegic and other patients with true or pseudo incontinence."[1] The bag capacity is 5 ounces up to the penile cone.

Should the capacity be insufficient to permit the patient to enjoy normal activities with peace of mind and complete comfort, any standard BARD Leg Bag can be easily attached. The top of the leg bag can be screwed on to the bottom of the urinal bag. For night use or bedside drainage, a rubber tube with threaded fitting is available.

The new McGuire Urinal is made with three belt sizes—all other dimensions are uniform . . . 508S—small, for waist size 26" to 32"; 508M—medium, for waist size 32" to 38"; 508L—large, for waist size 38" to 44". Price: each $8.50.

Now available from leading surgical supply houses throughout the country.

1. Bunts, R. Carl: A Practical Apparatus for Urinary Incontinence. J. Urology, 70: . . . (Sept.) 1953.

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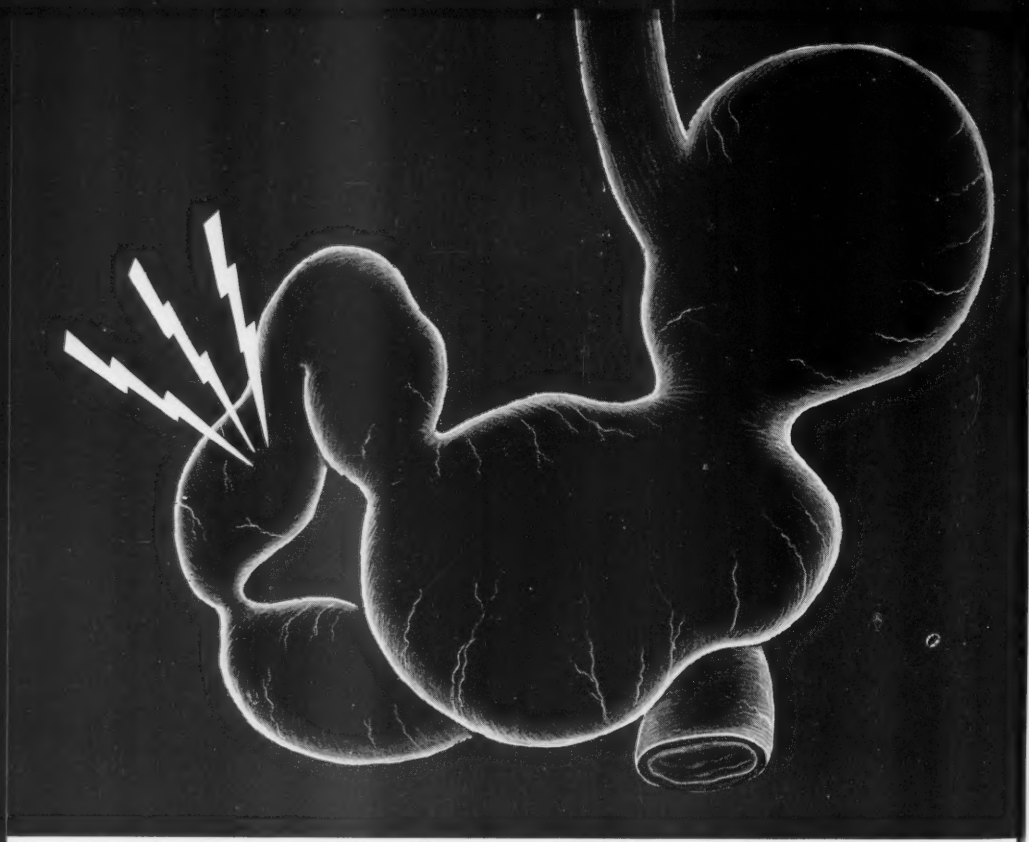
SUMMIT ***NEW JERSEY***



Abnormal Motility as the Cause of Ulcer Pain

Until recently the general opinion was held that ulcer pain was primarily caused by the presence of hydrochloric acid on the surface of the ulcer.

Present investigations[1,2] on the relationship of acidity and muscular activity to ulcer pain have led to the following concept of its etiologic factor:

> "...abnormal motility[2] is the fundamental mechanism through which ulcer pain is produced. For the production and perception of ulcer pain there must be, one, a stimulus, HCl or others less well understood; two, an intact motor nerve supply to the stomach and duodenum; three, altered gastro-duodenal motility; and four, an intact sensory pathway to the cerebral cortex."

Clinical Application of Pro-Banthine®

Pro-Banthine has been demonstrated consistently to reduce hypermotility of the stomach and intestinal tract and in most instances also to reduce gastric acidity. Dramatic remissions[1] in peptic ulcer have followed Pro-Banthine therapy. These remissions (or possible cures) were established not only on the basis of the disappearance of pain and increased subjective well-being but also on roentgenologic evidence.

Pro-Banthine (Beta-diisopropylaminoethyl xanthene-9-carboxylate methobromide, brand of propantheline bromide) has other fields of usefulness, particularly in those in which vagotonia or parasympathotonia is present. These conditions include hypermotility of the large and small bowel, hyperemesis gravidarum, certain forms of pylorospasm, pancreatitis and ureteral and bladder spasm.

1. Schwartz, I. R.; Lehman, E.; Ostrove, R., and Seibel, J. M.: A Clinical Evaluation of a New Anticholinergic Drug, Pro-Banthine, to be published.

2. Ruffin, J. M.; Baylin, G. J.; Legerton, C. W., Jr., and Texter, E. C., Jr.: Mechanism of Pain in Peptic Ulcer, Gastroenterology *23*:252 (Feb.) 1953.

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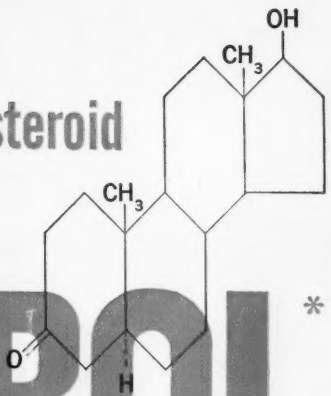
NEW crystalline steroid



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In female patients with advanced, inoperable carcinoma of the breast, Neodrol is as effective as testosterone—and may be somewhat better—in arresting progression, causing regression and preventing development of new lesions. Neodrol appears to offer some advantage over testosterone in alleviating symptoms.

Neodrol exhibits a relatively low incidence of virilizing side effects—unlike testosterone

The most distressing side effects of androgen therapy—hirsutism, acne, clitoral hypertrophy and increased libido—are less frequently encountered with Neodrol therapy and when present are usually slight in degree.

SUPPLIED: In multiple-dose (10 cc.), rubber-capped vials: 50 mg. per cc. *Trademark

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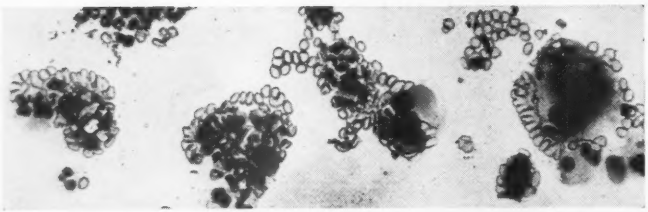
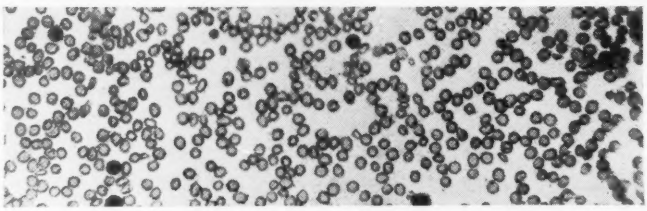
VISUAL PROOF

of the Unique Hematologic Action of Therapeutic Cobalt



Bone marrow showing—acquired erythrocytic hypoplasia—no nucleated erythrocytes.

Same patient showing—active erythropoiesis following cobalt therapy.



The photomicrographs illustrate the action of therapeutic level cobalt in producing actual regeneration of erythrocytes and their precursors even in severely *depressed human bone marrow.*

Because of extensive clinical studies with RONCOVITE—the original cobalt product—this understanding of direct stimulation of the depressed bone marrow has brought a completely new approach to the treatment of "secondary" anemia.

Roncovite provides a significant advance in the treatment of the great majority of *all* the microcytic and normocytic anemias commonly seen in practice.

In severe cases of anemia accompanying infectious and inflammatory disease, Roncovite may act so dramatically *as to make transfusion unnecessary*[2] while in prolonged "low grade anemia" it may simply overcome the erythropoietic inhibition which has prevented improvement in the blood picture.

Suggested Dosage: One tablet four times daily in adults; 0.6 cc. daily in infants.

RONCOVITE

DOSAGE FORMS

Roncovite Tablets—enteric coated, red, each contains cobalt chloride, 15 mg.; ferrous sulfate, 0.2 Gm.; bottles of 100.

Roncovite Drops—each 0.6 cc. contains cobalt chloride, 40 mg.; ferrous sulfate, 75 mg.; bottles of 15 cc. with calibrated dropper.

Write for literature and complete bibliography.

LLOYD BROTHERS, INC. **CINCINNATI 3, OHIO**

In the Interest of Medicine Since 1870

1. Case 2, Seaman, A. J., and Koler, R.: Acta Hematologica, 9:153, 1953.
2. Gardner, Frank H., J. Lab. Clin. Med.; 41:56, 1953.

MRT

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DIGITOXIN-Capsules-in-Oil,- 0.1 mg. (purple)
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1.0 cc. contains 194 mg. (3 grains)
Quinidine Sulfate, USP, in a special stabilizing, painless inert solvent.
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Liver, Yeast, Rice polishings, Wheat Germ and Honey!

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SERVICE TO MEDICINE-MRT

MRT

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VERASTAN TABLETS- 100 mg.
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Each teaspoonful (5 cc.) contains the total activity of Standardized Veratrum Viride-MRT, 100 mg. (One MRT Potency Unit). Available bottles of 8 fl. ozs., and 1 gallon.

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***Marvin R. Thompson and Robert E. Thompson: A. Ph. A., Scientific Section, Aug., 1953.
Cecil and Loeb: Eighth Edition (Saunders).
Conn: (Saunders), "Current Therapy",1953.

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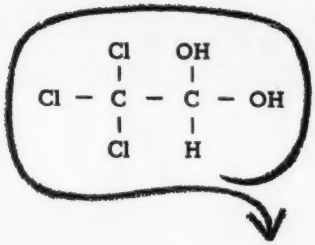

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3¾ gr. (0.25 Gm.) BLUE and WHITE CAPSULES
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Small doses of Chloral Hydrate (3¾ gr. Capsules Fellows) completely fill the great need for a daytime sedative. The patient becomes tranquil and relaxed yet is able to maintain normal activity.

DOSAGE: One 3¾ gr. capsule three times a day after meals.

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Restful sleep lasting from five to eight hours. "Chloral Hydrate produces a normal type of sleep, and is rarely followed by hangover."[1] Pulse and respiration are slowed in the same manner as in normal sleep. Reflexes are not abolished, and the patient can be easily and completely aroused . . . awakens refreshed.[2-3-4]

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EXCRETION—Rapid and complete, therefore no depressant after-effects.[3-4]

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1. Hyman, H. T.: An Integrated Practice of Medicine (1950)
2. Rehfuss, M. R. et al: A Course in Practical Therapeutics (1948)
3. Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics (1941), 22nd printing, 1951.
4. Soilman, T.: A Manual of Pharmacology, 7th ed. (1948), and Useful Drugs, 14th ed. (1947)

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three jumps ahead . . .

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To obtain maximum results, high salicylate blood levels are required. This means high oral dosage which can be attained, without excessive gastric disturbance, by using Salcedrox.

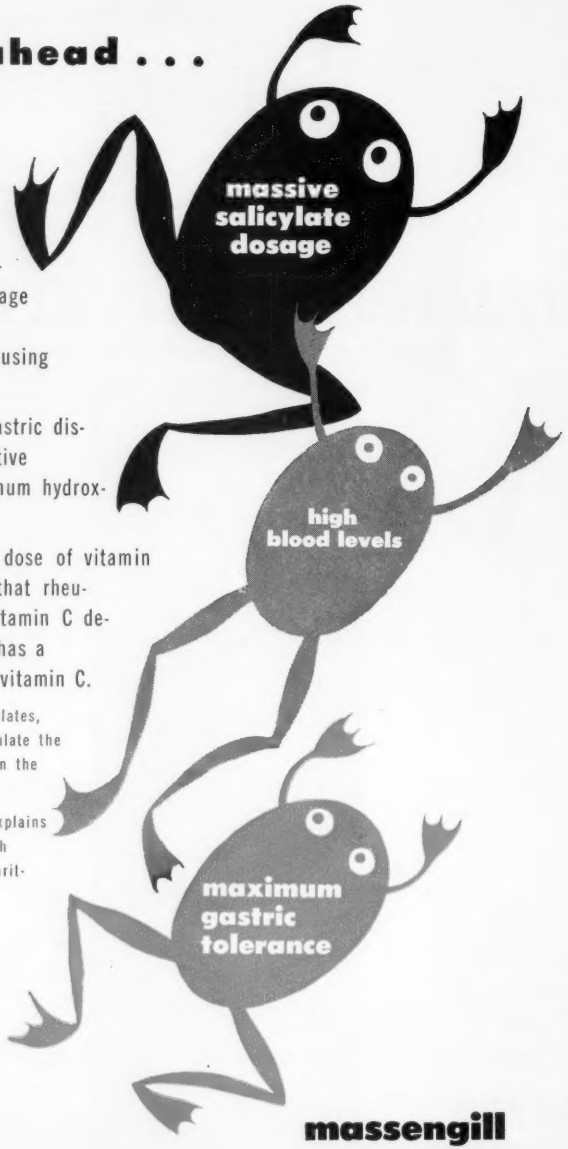
Salcedrox virtually eliminates gastric disturbance, because of the protective combination with activated aluminum hydroxide and calcium carbonate.

Salcedrox also contains a high dose of vitamin C, because it has been observed that rheumatic and arthritic states show vitamin C deficiencies, and salicylate therapy has a tendency to intensify depletion of vitamin C.

There is significant evidence that salicylates, through action on the hypothalamus, stimulate the pituitary, producing an ACTH- like effect on the adrenal cortex. *

This new concept of salicylate action explains many of the clinical results obtained with salicylate therapy in the treatment of arthritides and rheumatic afflictions—observed results that cannot be attributed to analgesic action alone.

*Proceedings Soc. Exp. Bio. Med., 1952, v80, 51-55, G. Cronheim, et al.



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Sodium Salicylate....5 gr. (0.3 Gm.)
Aluminum Hydroxide Gel. dried.....2 gr. (0.12 Gm.)
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IN THE TREATMENT OF HYPERTENSION

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FOR THESE CARDINAL REASONS:

- around the clock action—through the day and the night—from 4 doses per day...
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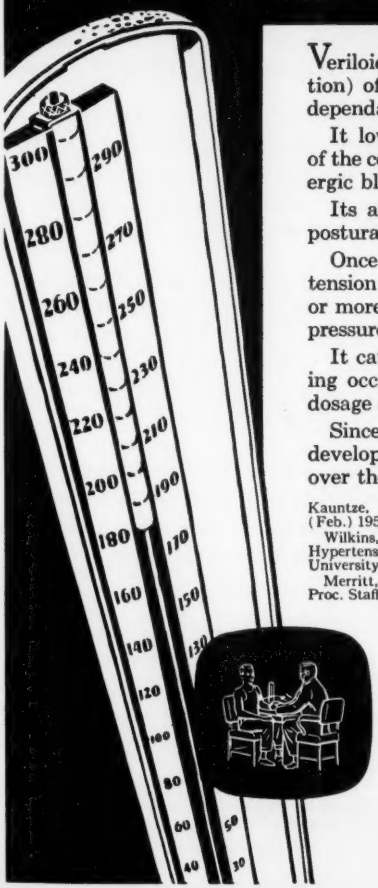

Veriloid, the selective alkaloidal extract (alkavervir fraction) of Veratrum viride, biologically assayed in dogs, is dependably uniform in potency and action.

It lowers blood pressure promptly through mediation of the central nervous system, without ganglionic or adrenergic blockade. Not a local vasodilator.

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Once dosage is established, prolonged control of hypertension is possible. Even after nine months' therapy 30% or more of patients retain the induced reduction in blood pressure—a notably high percentage.

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Since action is not cumulative, since tolerance does not develop, Veriloid is excellently suited "for the long pull" over the years.

Kauntze, R.: Veratrum and Its Derivatives, The Practitioner *170*:189 (Feb.) 1953.

Wilkins, R. W.: Recent Experiences with Pharmacologic Treatment of Hypertension, in Bell, E.T.: Hypertension, A Symposium, Minneapolis, University of Minnesota Press, 1951, p. 492.

Merritt, W. A.: The Treatment of Essential Hypertension with Veratrum, Proc. Staff Meet. Mayo Clin. *27*:481 (Nov. 19) 1952.

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VERILOID is supplied in slow-dissolving scored tablets, in 2 and 3 mg. potencies. Initial recommended dosage, 9 mg. daily, in divided doses, not less than 4 hours apart, preferably after meals. Maintenance dose, 9 to 24 mg. per day.

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SIX fundamental reasons Why BOBST PHARMACAL

OUR PURPOSE

Everyone was talking about geriatrics – but prior to the organization of BOBST PHARMACAL in the fall of 1949, there was no pharmaceutical house devoted to the exclusive interest of geriatrics. BOBST did it!

THE CHALLENGE

Senescence and a rapidly increasing aging population present a challenge. It is estimated that over 30% of our population, nearly 50,000,000 people, fall in the "over 40" age group, requiring specialized care and treatment to prevent the casualties of the 60's.

OUR MANUFACTURING ROLE

BOBST supplies those products especially designed to help combat the chronic, crippling and degenerative diseases of the older patient. BOBST is a pioneer name in the early large scale manufacture of synthetic vitamins and sex hormones and continues in the pioneering of modern chemotherapeutic remedies.

OUR RESEARCH ROLE

Parenteral medication has proved the value of multiple therapeusis, impossible in the past with oral medication because of poor absorption from the gastrointestinal tract. BOBST spent thousands of dollars to develop BOSEAL type oral medications with their multiple, separate coats to insure ingredient stability and absorption in effective multiple therapy.

OUR PROFESSIONAL ROLE

BOBST products always reflect uniform potencies–quality controls and assays from raw materials to finished products. BOBST prescription specialties are distinctive, outstandingly exclusive (the majority are original "firsts on the market") and confirmed by clinical performance.

OUR FUTURE ROLE

The demands of geriatric care are new and challenging. New products must fit comfortably into the patient's limited budget. BOBST pharmaceuticals are the first to permit a practical, economical and more hopeful approach towards "staying the hands of time."

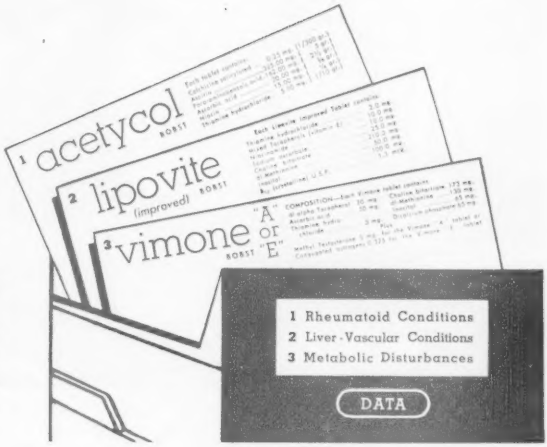
BOBST meets the challenge with a broad research program including cooperative studies with independent laboratories, clinics, universities and other progressive research centers. The BOBST Awards in Gerontology, another form of research stimulation, were first made at the Second International Congress of Gerontology held in St. Louis in the fall of 1952, upon recommendation of a special committee of the International Gerontological Association.

"BOBST"—THE FIRST NAME IN GERIATRICS!

YESTERDAY—inspired by the basic conviction that "a genuine need existed," BOBST became the *first name* in pioneering the early (1930's) *large scale* basic-pharmaceutical manufacture of the *synthetic vitamins* and *sex hormones.*

TODAY—inspired by the same basic conviction BOBST is forging another *new* and *vital link* between pharmaceutical manufacturer and the physician, by *pioneering* the manufacture of medicinal agents of special therapeutic value in combatting the chronic diseases and degenerative states—conditions recognized as medicine's No. 1 problem.

This is well illustrated by the three distinctive and outstandingly original BOBST PRODUCTS described on this page.



1. ACETYCOL—

a multicoated tablet manufactured by the special BOSEAL process, containing salicylic acid, salicylated colchicine, para-aminobenzoic acid, ascorbic acid, niacin, and thiamine hydrochloride in balanced amounts has been found invaluable in controlling the pain and giving symptomatic relief to the patient with arthritis.

DOSAGE: 1-4 tablets daily.

HOW SUPPLIED: Bottles of 100, 500 and 1,000 tablets.

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a carefully balanced lipotropic-vitamin with B_{12} preparation offers a particularly flexible dosage form of lipotropes, supported by generous amounts of the major essential vitamins, ordinarily only available by a separate prescription. A real prophylactic agent for "heading-off" the preventable aspects of beginning aging.

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HOW SUPPLIED: Bottles of 60, 120 and 1,000 tablets.

3. VIMONE—

either with an *Androgen ("A")* or with an *Estrogen ("E")* and containing three lipotropic factors, three of the most essential vitamins along with fortifying amounts of calcium has found an increasingly important place in treating the "over 40" patient with symptoms pointing towards climacteric change and often early liver-vascular disorders.

DOSAGE: 1-3 tablets daily of either "A" or "E" as indicated.

HOW SUPPLIED: Boxes of 20, 50, and 100 tablets.

Kindly address professional inquiries, sample requests to office nearest you on the following Bobst products:

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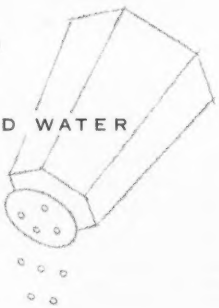

PRESCRIBE NEOHYDRIN whenever there is retention of sodium and water except in acute nephritis and intractable oliguric states. You can balance the output of salt and water against a more physiologic intake by individualizing dosage. From one to six tablets a day, as needed.

PRESCRIBE NEOHYDRIN in bottles of 50 tablets. There are 18.3 mg. of 3-chloromercuri-2-methoxy-propylurea in each tablet.

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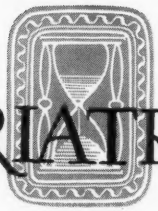

Formation of a Third Coronary Artery by Internal Mammary Artery Implant

Arthur Vineberg, M.D.

In 1772, Heberden first reported the occurrence of certain types of chest pains which he named *angina pectoris*. He had no knowledge of its pathologic basis, and seemed to be unaware of this syndrome's relationship to heart disease.

More recently, angina pectoris has been identified with reversible myocardial ischemia. An overworked myocardium, with an inadequate blood supply, is said to develop pain in the same manner as an ischemic skeletal muscle. Current opinion holds that angina pectoris occurs only when coronary artery narrowing or occlusion is present. It is, however, only one of the symptoms associated with coronary artery insufficiency.

Early attempts at surgical treatment of angina pectoris were directed at the relief of this symptom complex by various nerve sectioning procedures. However, during the past seventeen years, led by the work of Claude Beck and sparked by the tremendous development in thoracic surgery, many efforts have been made to increase the coronary circulation. The various surgical procedures which have been described may be grouped according to the manner in which the arterial blood is brought to the ventricles.

SURGICAL PROCEDURES TO INCREASE CORONARY CIRCULATION

1. *Surface of ventricles*

   a. *Grafts.* The first method attempted was to bring arterial blood to the

ARTHUR VINEBERG, *a graduate of McGill University School of Medicine in 1928, specializes in cardiothoracic surgery in Montreal, where he is a lecturer in surgery at McGill, a member of the surgical staff of Royal Victoria Hospital, chief surgeon at Grace Dart Home Hospital, and director of cardiothoracic surgery at Jewish General Hospital. He is the author of numerous articles in the field of thoracic surgery.*

surface of the ventricles. This has been accomplished by means of grafts, such as pectoral muscle, omentum, lung, and skin. In these procedures, the graft is sutured to the surface of the left ventricle. In this way, it was hoped that new blood vessels would grow from the graft into the ventricular myocardium and thereby supply it with fresh arterial blood.[1, 2]

b. *Cardiopericardiopexy.* Another method of bringing fresh blood to the ventricular surface is by the creation of granuloma between the parietal and visceral pericardium. This was first attempted by Beck, using a burr beef bone and finally asbestos powder.

Others such as Thompson, have placed various irritating substances into the pericardial sac. The most favorable of these is powdered talc.

Thompson[3] has reported having performed cardiopexy on a series of patients; the first is now thirteen years after operation. He is of the opinion that this procedure has been helpful in rehabilitating a group of cardiac cripples. The procedure is simple and may be of value in helping incapacitated patients who are unable to undergo more extensive surgery.

2. *Cardiac vein ligation*

By cardiac vein ligation, Fauteux[4] thought that interarterial anastomoses would be opened and that the ventricle would receive increased oxygenation by means of the thebesian canals. Fauteux performed this operation on human cases of coronary artery insufficiency, but the results are not too well known due to Fauteux's sudden death.

3. *Arterialization of the coronary venous system*

A completely new approach to the problem was devised by Beck[5] who anastomosed the aorta to the coronary sinus by a vein graft. By this method, fresh arterial blood is sent into the coronary sinus along the coronary veins. There are two operations, three to four weeks apart. At the first operation, the aorta is anastomosed to the coronary sinus by means of a vein graft; at the second operation, the coronary sinus is partially tied proximal to the vein graft. In this way, arterial blood is forced into the coronary venous system. Its disadvantages are: (1) Technically, the venous graft is difficult to place and requires two separate operations, ten days to three weeks apart. (2) A high percentage of venous grafts are found to be thrombosed at the second stage. (3) An arteriovenous aneurysm is artificially produced. (4) Vein grafts tend to balloon out after a few years. (5) There are other veins besides the coronary sinus which drain the left ventricle. These empty directly into the right auricle. Thus, when arterial blood is directed into the coronary sinus in a retrograde fashion, eventually a large part of it should find its way back into the right auricle along normal venous channels. Some may go directly into the heart chamber via the thebesian canals.

4. *Internal mammary arterialization of left ventricular muscle*

In this procedure, the left internal mammary artery is detached from its position beneath the sternum and implanted into the left ventricular myocardium, with one or more attached open and bleeding intercostal arteries

(figure 1). In its new position, the artery sends out new arterial branches which join with the small coronary arterial vessels within the ventricular myocardium. Through these, fresh arterial blood is delivered to the myo-

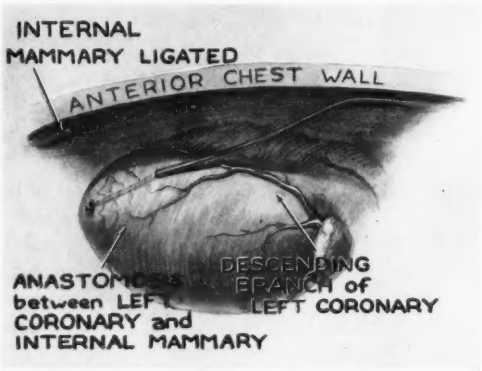

FIG. 1. Drawing of internal mammary artery lying in the anterior wall of the left ventricle after it has been detached from the chest wall. Note how the artery in its new position sends out branches which join with those of the left coronary artery.

cardium. Thus, the implanted internal mammary artery literally forms a third coronary artery to the heart.

Internal mammary artery arterialization of the left ventricle is based upon the following anatomical, physiological, and pathological facts:

The anatomical structure of the myocardium differs greatly from other muscular structures in the body. Lying between and around myocardial fibers there is a veritable sponge-work of vessels[6] which vary in size from arterioles down through the sinusoids to the capillaries. These are graphically shown in figure 2. The coronary circulation is a peculiarly rich sponge-work of

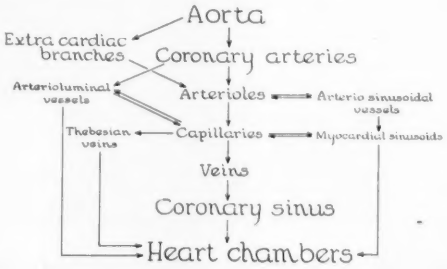

FIG. 2. A graphic outline of the relationship between sinusoidal arterial vessels, myocardial sinusoids, and capillaries.

vessels between and around the myocardial fibers. This may explain why an internal mammary artery placed within the myocardium fails to thrombose and remains open in 80 per cent of our animals. Continuous blood flow down the implanted artery is probably maintained because blood is allowed to escape through the attached open intercostal vessels. Since myocardial hematomas are never formed, we believe the artery bleeds directly into the myocardial sinusoidal sponge-work, which carries the blood away.

We have shown the development of anastomosis between an implanted internal mammary artery and the left ventricular coronary arterial system. This has been proved by injection, x-ray films, serial sections, and digestion cast studies.

MAMMARY-CORONARY ANASTOMOSIS

Anatomic proof

Schlesinger's[7] solution has been used as the injection mass because it is said to penetrate nothing smaller than 40 microns. The internal mammary artery is implanted into the left ventricular myocardium (figure 1). Six weeks to fifty-eight weeks later, when the animal is sacrificed, the heart and its attached internal mammary artery are removed from the body and placed in a warm saline bath. A cannula is inserted into the internal mammary artery facing toward the heart. Another cannula is tied into the left coronary artery. The injection mass is introduced through the cannula in the internal mammary artery (figure 3). When there is an anastomosis between the internal mammary artery and the left coronary vessels, the injection mass is seen to quickly fill the vessels of the left ventricle and to emerge from the cannula which was placed in the left coronary artery. After injection, the heart is x-rayed to show the vessels filled with the radiopaque Schlesinger's injection mass (figure 4).

FIG. 3. Photograph of heart of animal 185 N after injection through the internal mammary artery 7 weeks after implantation. This animal survived anterior descending and circumflex artery ligation. The injection mass was introduced through the implanted internal mammary artery (lower left) and spread out over the heart to emerge from the glass cannula tied in the mouth of the left coronary artery (upper right). This has occurred regularly, and suggests that the implanted internal mammary artery joins with the coronary arterial rather than with the venous circulation.

When the heart has been x-rayed, serial sections are taken through the site of internal mammary artery implantation. This has been done in many animals when there was evidence of anastomosis. In each case the arterial branches leaving the implanted internal mammary artery have been traced out into the myocardium (figure 5).

Duration of coronary-mammary anastomosis

Recently, Glenn and associates confirmed the development of an anastomosis between an implanted internal mammary artery and the coronary vessels.

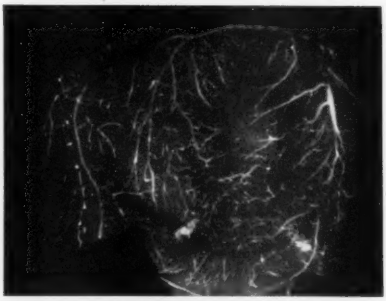

FIG. 4. Radiograph of unrolled heart of animal No. 7 M. This animal survived ligation of anterior descending branch of left coronary artery 93 days after internal mammary artery implantation. It was sacrificed 115 days later and the internal mammary artery injected with radiopaque Schlesinger's solution. Note how injection mass entered the 7-months-old implant to fill the coronary arterial system of both left and right ventricles.

However, they stated that the new vessels tend to disappear at the end of eight weeks. They further suggested that the new vessels were small and resembled granulation tissue.

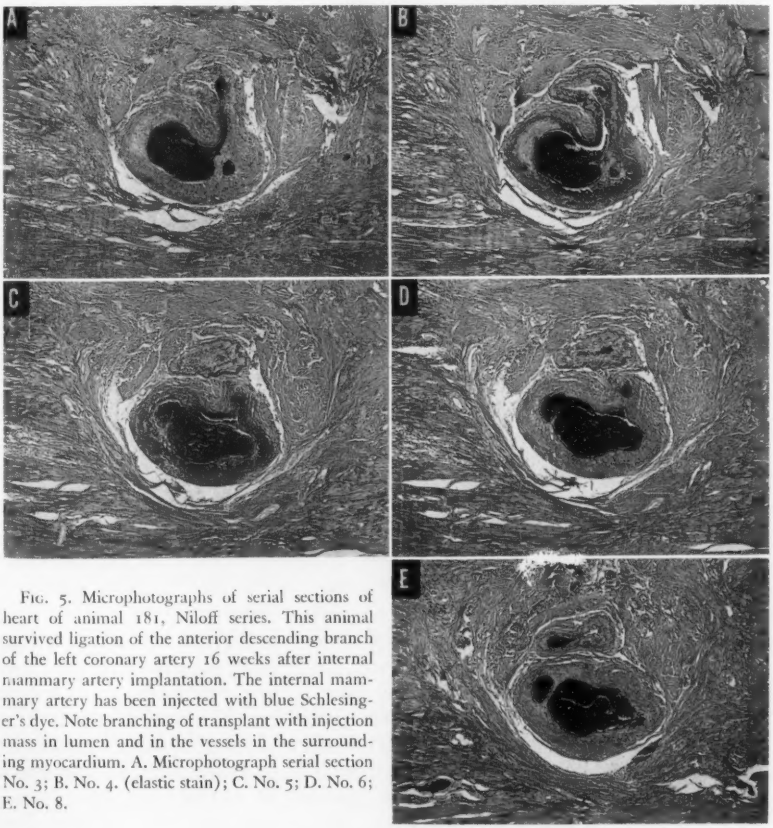

FIG. 5. Microphotographs of serial sections of heart of animal 181, Niloff series. This animal survived ligation of the anterior descending branch of the left coronary artery 16 weeks after internal mammary artery implantation. The internal mammary artery has been injected with blue Schlesinger's dye. Note branching of transplant with injection mass in lumen and in the vessels in the surrounding myocardium. A. Microphotograph serial section No. 3; B. No. 4. (elastic stain); C. No. 5; D. No. 6; E. No. 8.

In our series, the average interval from implant to sacrifice was eleven weeks (table 1). Some animals were kept fifty-eight weeks after implantation. The anastomoses at the end of that time not only persisted, but were large enough to protect against death and infarction following ligation of the anterior descending branch.

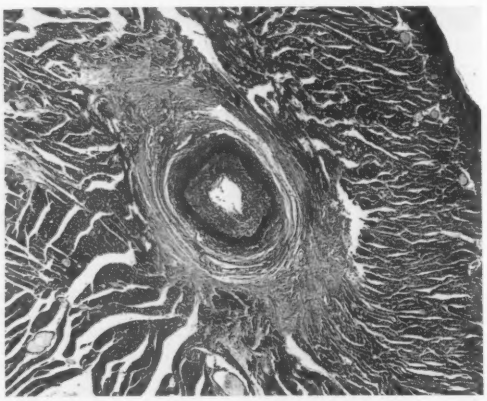

FIG. 6. Section of internal mammary artery of animal 8 V, 122 days after implantation, stained with special stains to show muscle and elastic tissue.

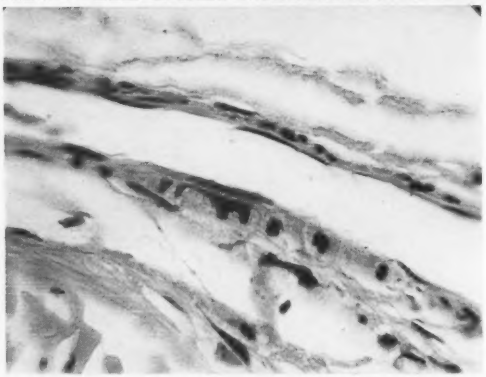

FIG. 7. High power view of a branch of the internal mammary artery shown in figure 13. This branch has been traced from the implanted internal mammary artery into the myocardium. Special stains show that its walls are composed of muscle and elastic tissue.

Character of coronary-mammary anastomosis

Not only has it been suggested that the coronary-mammary anastomosis tends to disappear at the end of eight weeks, but it has also been suggested that the anastomosis is capillary in character. Serial section studies of 7 implants have been examined. Special stains of these serial sections have been made to show elastic and muscle tissue. The character of the new branches formed by the internal mammary artery implant have thus been studied. They have been found to be arterial in nature, containing both muscle and elastic tissue in their walls. These new arterial branches have been followed by serial section far out into the myocardium until they disappear (figures 6 and 7).

Visualization of mammary-coronary anastomosis

From our injection studies there seemed little doubt that the internal mammary artery after implantation into the left ventricular myocardium sends out true arterial branches which join with the arterial branches of the left coronary system. However, to more clearly demonstrate the nature of the mammary-coronary anastomosis, corrosion casts have been made by injecting the implanted internal mammary artery with a plastic substance from six days to three months after implantation. The plastic used resists both acid and alkaline digestion. When there was a mammary-coronary anastomosis, it was possible to obtain a cast of the entire left coronary arterial structure by injecting the plastic into the implanted internal mammary artery. In the cast shown in figure 8, as in others, the entire coronary

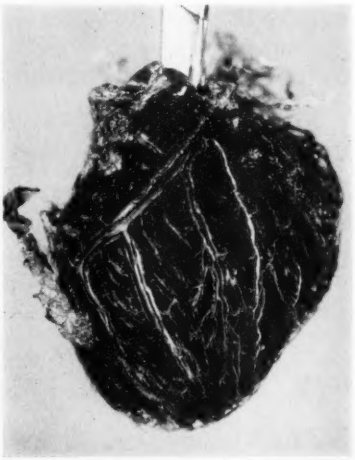

FIG. 8. Corrosion cast made by injecting the internal mammary artery in an animal, 3½ weeks after implantation, with a plastic substance which resists both acid and alkaline digestion. Note how the left coronary arterial network has been filled out by the plastic. The structure on the left is the internal mammary artery. The lighter colored vessels are branches of the anterior descending branch of the left coronary artery which have been filled with the plastic. They are lighter only because the dye had faded by the time the photograph was taken.

arterial tree has been filled and shows up as a vast sponge-work of vessels after the heart muscle has been removed by digestion. The vessels filled by injecting the implanted internal mammary artery resemble in every way those outlined in a control heart by injecting the left coronary artery alone.

From the foregoing it is evident that the internal mammary artery after implantation into the left ventricular myocardium forms an anastomosis with the arterial side of the left coronary circulation. The anastomosis is not capillary in nature, but is formed by the joining together of arterioles. It does not tend to disappear in a few weeks, and has been found to be present more than a year later.

Frequency of mammary-coronary anastomosis

In previous publications the factors influencing anastomosis and the frequency of its occurrence have been discussed.[8-14] Generally, the implanted artery remains patent in 80 per cent of implants. However, large mammary-

coronary arterial anastomoses have been demonstrated in from 50 to 75 per cent of implants, depending on the type of experiment. It has always been

TABLE 1
DURATION OF ANASTOMOSIS

Type of Anastomosis	*No. of Animals*	*Presence of Anastomosis After Implant (weeks)*	*Value of Anastomosis After Ligation of Anterior Descending Branch of the Left Coronary Artery*
Microscopic Anastomosis	1	5	
	1	6	
	1	7	
Anastomosis small due to thickened or partially thrombosed internal mammary artery	2	8	Protection against death or infarction afforded in 3 animals only
	2	11	
	2	12	
	2	13	
	1	14	
	12		
Macroscopic Anastomosis	1	6	No deaths or infarction occurred
	2	7	
	5	9	
	5	11	
Anastomosis large	4	12	
	2	14	
	1	17	
Internal mammary Artery patent	1	18	In cellophane coronary artery sclerosis, caused by cellophane irritation, marked improvement in exercise tolerance occurred
	3	19	
	1	21	
	1	31	
	1	41	
	1	46	
	1	58	
	29		

higher in those experiments where the internal mammary artery is implanted not into a normal heart but into one which has been previously or simultaneously rendered ischemic.

Functional value of mammary-coronary anastomosis

Histoanatomic proof of the development of anastomotic channels between extracardiac arterial sources and the coronary circulation gives no indication of its functional value. The demonstration of the existence of anatomic arterial pathways between extracardiac and coronary arterial vessels does not prove the direction of blood flow. It is possible that the direction of blood flow could be from the coronary circulation toward the extracardiac source. This is not only true of mammary-coronary anastomosis but is true of all other types of procedure used for augmenting myocardial circulation.

FUNCTIONAL TESTS FOR NEW ARTERIAL BLOOD SUPPLY

1. *Survival experiments following ligation of the anterior descending branch of the left coronary artery*

There is some divergence of opinion in the literature as to the effects of ligation of the anterior descending branch of the left coronary artery. There

are those who claim a low mortality for this procedure, and others who claim a high mortality. The majority of investigators have found that the mortality in dogs ranges from 70 to 80 per cent. In our series of 10 control dogs, the average mortality rate from anterior descending branch ligation was 80 per cent.

Method of ligation

The anterior descending branch of the left coronary artery should be ligated at its origin. The position of the ligature must be carefully checked by examining the left coronary artery to make certain that the ligature has included all branches other than the circumflex. Frequently one or two septal branches are missed and occasionally branches arise directly from the main trunk of the left coronary artery.

An analysis of the results of anterior descending branch ligation is shown in table 2. A total of 78 dogs had anterior descending branch ligation. There were 10 control animals and 39 other animals in whom the coronary circulation was not augmented. In this group of animals there was an overall 80

TABLE 2
EXPERIMENTAL DATA
(Vineberg and co-workers)

	Ligation Anterior Descending Branch of the Left Coronary Artery			
	No. of Dogs	*Death*	*Survival with Infarction*	*Survival without Infarction*
Control	10	80%	20%	0
Internal mammary artery implant and/or other experiments but without augmentation of the coronary circulation	39	80%	3%	17%
Internal mammary artery implant with coronary anastomosis	29	....	....	100%

Note: Internal mammary artery after implantation forms anastomoses with coronary circulation in from 50 per cent to 75 per cent of animals operated upon.

per cent mortality with a 20 per cent survival with infarction. In 29 animals in whom large mammary-coronary anastomosis had developed there were no deaths and no infarctions following anterior descending branch ligation. Thus it would seem that coronary-mammary anastomosis not only increases coronary circulation but gives protection against death and infarction.

The experimental data shown in table 2 indicates that coronary-mammary anastomosis when it occurs is of value in protecting against death or infarction. However, because of the difference of opinion concerning the value of survival after anterior descending branch ligation, a second group of functional experiments were performed.

2. Direction of blood flow in implanted internal mammary artery

The direction of blood flow through the implanted internal mammary artery was studied in order to determine whether it was bringing blood to the ventricular myocardium. Direct determination of the direction of blood flow in the internal mammary artery was difficult, so the indirect method was used. Animals which survived anterior descending branch ligation of

the left coronary artery were subjected four to five weeks later to complete and sudden occlusion of the implanted internal mammary artery. If the internal mammary artery was maintaining the circulation of the left ventricle then following its ligation either death or infarction should result. This is exactly what happened. In 3 animals with an internal mammary implant which had survived anterior descending branch ligation, the internal mammary artery was ligated. One animal died within twenty-four hours, and displayed an edematous cyanotic area of the anterior wall of the left ventricle. One survived for three days before dying from a large infarct in the same location (figure 9). The third animal survived, but examination of the sacrificed specimen revealed that multiple intercoronary anastomoses were present.

In all of these animals there was a demonstrable mammary-coronary artery anastomosis. In those animals that died following internal mammary artery ligation there can be little doubt that the circulation of the anterior portion of the left ventricle was being maintained by the internal mammary artery implant. The evidence just presented suggested that the internal mammary artery after implantation into the left ventricular wall is capable of maintaining the left ventricular circulation. These experiments, however, were carried out on the hearts of normal animals. It was therefore necessary to attempt to artificially produce coronary artery insufficiency and to treat it by internal mammary artery implantation.

Thus, we set out to experimentally produce and treat coronary artery insufficiency and so establish a third functional test of the value of an internal mammary-coronary anastomosis.

3. *Experimental production and treatment of coronary artery insufficiency*

In this series of experiments coronary artery insufficiency was produced in dogs and treated by internal mammary artery implant. The first problem

FIG. 9. Photographs of heart of animal 10, series A, Group B (Miller). This animal withstood anterior descending branch ligation 67 days after internal mammary artery implant. Thirty-six days later the thorax was reopened and implanted mammary artery was ligated resulting in ectopic beats and cardiac irritability. The animal died 3 days postoperatively. A large 3 x 3 cm. anterior wall left ventricular infarct was found. Perfusion of the internal mammary artery showed free communication between the implant and the left coronary tree, but not the right.

was to find a method of producing coronary artery occlusion which would simulate that which occurs in human coronary sclerosis.

The second problem concerned the evaluation of coronary insufficiency when it was produced, and its response to treatment.

Method of producing coronary artery insufficiency

The anterior descending branch of the left coronary artery was exposed at its origin. Beneath the left auricular ventricular sulcus to the left of the pulmonary trunk the epicardium overlying the vessel was incised and the bifurcation of the main coronary artery exposed. A doubly folded strip of cellophane (DuPont P.T.—300) sterilized for twenty-four hours in a saturated solution of mercury oxycyanide was twice wrapped completely but loosely around the origin of the anterior descending branch of the left coronary artery and fixed in position. Thus a segment of artery from 4 to 8 mm. long was completely surrounded with cellophane.

The cellophane initiated a fibroplastic reaction with collagen deposition about the artery. As subsequent contracture of the new fibrous tissue occurred, the lumen of the anterior descending branch of the left coronary artery was slowly narrowed. Gradually that portion of the myocardium nourished by this vessel became ischemic.

At the end of the experiment, when the animals were sacrificed, the anterior descending branch of the left coronary artery was probed to determine the extent of narrowing. Sections were made through the artery at the site of the cellophane wrap and careful histologic studies made of the degree of coronary occlusion (figure 10).

Method of evaluation of experimentally produced coronary insufficiency and its treatment

Exercise tolerance test. In human coronary artery insufficiency there are two outstanding symptoms, namely, substernal pain and intolerance to exercise. In the dog, it is most difficult to detect the presence of pain. It is, however, not difficult to accurately determine the animal's tolerance or intolerance to exercise.

Clinical and pathologic experience has associated progressive exercise intolerance with progressive myocardial ischemia. Thus in the experimental animal, progressive diminution of exercise tolerance has been accepted as evidence of myocardial ischemia. In this series of experiments, myocardial ischemia was produced by a cellophane wrap placed around the origin of the anterior descending branch of the left coronary artery. Exercise tolerance studies were carried out before and after cellophane wrap. Later, after internal mammary artery implant, they were repeated in order to establish if improvement had occurred.

A treadmill was used to exercise the animals. This was made originally for man and was thus very satisfactory for exercising large animals. The treadmill consisted of an endless leather belt mounted between two electrically driven steel drums. The available exercising platform was approxi-

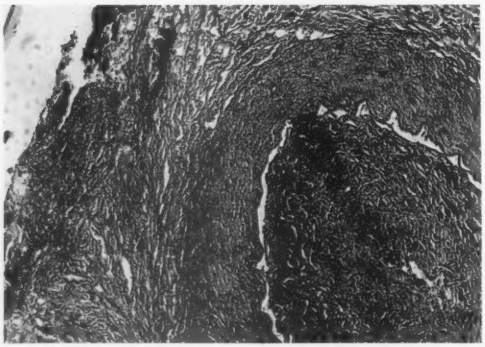

FIG. 10. Section through the anterior descending branch of the left coronary artery of animal 185 M. Series showing degree of occlusion of arterial lumen produced by sclerosing type cellophane Dupont PT-300.

mately 8 feet by 2 feet in diameter. The movement of the belt could be controlled and a clocking device continuously registered the speed in miles per hour. In this way, a controlled quantity of exercise could be administered for any required time. The dogs were led on to the movable platform and encouraged while the mechanism was set slowly in motion. The speed was gradually increased until the dogs were running at a rate comparable to 8½ miles per hour. The exercise was continued until the animals became exhausted or ceased to run because of distress. The average running time for the animals before operation, or presumably before the development of myocardial ischemia, was nine to twelve minutes at 8½ miles per hour. At this time the animals became tired and began to lag on the mill and would break alternately from a gallop to a run. Eventually the animals became anxious to escape the mill and exercise was discontinued. Such animals would avidly drink water. In three to four months after the cellophane was placed about the anterior descending branch of the left coronary artery the dogs would tolerate only two to four minutes of exercise before becoming extremely anxious, whining and salivating profusely. If the mill was not stopped they would attempt to lie down or drag their feet on the revolving belt. When the exercise was stopped they would drop where they stood and for some minutes resist all coaxing to move; they showed no interest in drinking water. When these latter symptoms developed, electrocardiographic changes indicative of myocardial ischemia were apparent. It was thus postulated that the decrease in exercise tolerance was due to the development of myocardial ischemia and that the acute symptoms displayed by these animals was the canine counterpart of human angina pectoris.

Twenty-five dogs were trained on the treadmill, their running time recorded, and they were subsequently operated upon. Cellophane, DuPont P.T.—300, was wrapped around the first 1.5 cm. of the anterior descending branch of the left coronary artery. Ten of these animals survived the procedure, the remainder died of ventricular fibrillation at the time of operation, or postoperatively from pneumonia, empyema, or distemper. After these animals had satisfactorily recovered from surgery their exercise tolerance was periodically determined.

Of the 10 surviving animals, 4 were kept for control studies, the remaining 6 had an internal mammary artery implant after their exercise tolerance had been reduced from nine to twelve minutes to two-and-a-half to four minutes. This occurred approximately three months after cellophane wrap. Only 3 animals of the 6 survived the internal mammary implant procedure. One animal died of distemper; 2 animals died of empyema.

After recovery the 3 surviving animals were again exercised periodically, and three to five months after the implant operation, the exercise tolerance of 2 of these animals was six and eight minutes, respectively, whereas the 4 control animals together had an average exercise tolerance of 1.6 minutes. All three of the implanted animals showed evidence of a large internal mammary-coronary anastomosis. The one animal whose exercise tolerance did not improve after implant was found to have a large substernal abscess. This presumably accounted for its failure to increase its tolerance after implant. Careful studies and sections were made of the site of the cellophane wrap, and injection studies were carried out by the previously described technics.

Another group of experiments was carried out in which the cellophane wrapping procedure was performed simultaneously with the internal mammary artery implant. In this group there were 6 animals, 1 of which died postoperatively from pneumonia. The 5 surviving animals were studied for four months. Two animals had a reduction in exercise tolerance to two to three minutes, respectively. At sacrifice these animals showed no significant internal mammary-coronary anastomosis. The exercise tolerance of the remaining 3 animals was maintained at slightly below preoperative levels.

When these animals were sacrificed, 2 were found to have widely patent internal mammary-coronary anastomosis. The remaining animal was found to have developed an anastomosis with the coronary venous circulation. This was the first instance in which this had occurred in our experience. The anterior descending branch of the left coronary artery in all of these animals showed marked narrowing at the site of the cellophane wrap (figure 10).

CLINICAL APPLICATION OF THE IMPLANT PROCEDURE

On the basis of the foregoing anatomical and functional evidence, the treatment of human coronary artery insufficiency was considered.

When this work was first started in 1945, coronary artery disease was generally considered a hopeless condition for surgical treatment. Most cardiologists held that the coronary arteries throughout the heart were diseased and therefore attempts at revascularization were futile. Pathological studies of hundreds of cases of coronary disease unfolded a different picture. Schlesinger[15] and others pointed out that the disease was usually confined to the epicardial vessels and rarely, if ever, involved the vessels deep in the myocardium. Thus, in coronary artery disease there lies within the myocardium a network of healthy coronary vessels capable of carrying blood to the myocardial fibers. It is into such a network of vessels that we proposed and have introduced an internal mammary vessel.

Selection of patients

The selection of patients for a new procedure is always difficult. Although we dislike classifications, we have found it convenient to divide our cases of coronary artery insufficiency into three groups:

Group 1—Mild or intermittent angina

In this group are those patients who experience an occasional attack of anginal pain on exercise, or during an emotional disturbance. They are able to work, and are capable of living reasonably normal lives.

Group 2—Status anginosus

In this group are patients who experience angina at rest. They literally chew nitroglycerin tablets day and night. One of our patients in this group consumed 180 nitroglycerin tablets in two weeks. This type of patient should not be submitted to cardiac surgery. There is insufficient cardiac muscle left to revascularize. Generally, these patients are living on a pinpoint opening in the one artery which is still open. Such a small vessel cannot supply sufficient blood to the myocardium to keep the patient alive during and after a major intrathoracic procedure.

Group 3—Disabled, but without angina at rest

Patients in this group may or may not be able to work part-time. Pain, fatigue and dyspnea make life intolerable. If such patients can walk 50 to 100 feet without pain, and if there are no contraindications, they are suitable for internal mammary artery implantation. In this group are included patients with one or more coronary artery occlusions with infarction.

With each patient we have attempted to exclude all other causes for his symptoms. This has been done in spite of a well established diagnosis of coronary artery insufficiency. Thus, a search is made for intervertebral disks, infra- and supra-diaphragmatic lesions and, in most cases, a psychiatric screening is done.

Contraindications include (1) the history or evidence of left ventricular failure; (2) enlargement of the left ventricle, unless it is due to hypertrophy associated with moderate hypertension; (3) advanced cases of essential hypertension; (4) evidence of a recent myocardial infarction (six months' delay is advisable in such patients); and (5) status angina.

This report deals with our experience with 9 patients with coronary artery insufficiency who have undergone internal mammary artery implantation in the past three years. Some of the facts concerning each patient are shown in table 3.

All of these patients were males. Their ages varied from 46 to 57 years. The majority were over 52. All were unable to work at the time of operation. Their periods of disability varied from seven to thirty-six months.

Of these 9 patients, 7 had one or more proven myocardial infarctions. Anginal pain was not the only symptom. In 6 of these cases, dyspnea on effort, and in 3, fatigue, were prominent symptoms. Exercise tolerances varied from 50 to 200 feet on the level and were markedly lowered in the two-step test.

Operative technic

Prior to operation, the range of apical movement is determined by fluoroscopic examination, and the position of the apex ascertained during quiet

respiration. The location of the apex determines whether the fifth or sixth rib is resected on the left side. The internal mammary artery must be sufficiently freed from the chest wall so that after its insertion into the left ventricle there is enough slack to allow for apical movement during respiration.

The patient is placed in the right lateral position. The pleural cavity is entered after resection of either the fifth or sixth rib. The lung is packed

TABLE 3
NO ANGINA AT REST

					Anginal Pain					
Name	*Sex*	*Age*	*Occupation*	*Time Disabled (months)*	*At Rest*	*Amount Exercise*	*Eating*	*Night*	*Dyspnea*	*Fatigue*	*Previous Infarction*
D.M.	M	54	Oil field worker	7	No	150 ft.	Yes	No	Yes	Yes	None
E.S.	M	49	Executive	24	No	100 ft.	Yes	No	Yes	No	Anterior Posterior
C.A.	M	55	Machinist Welder	24	No	150 ft.	Yes	No	No	No	Large anterior
A.M.	M	55	Grocer	10	No	50 ft.	Yes	No	Yes	Yes	None
S.E.	M	57	Electrician	10	No	50 ft.	No	No	No	No	Large anterior
G.A.	M	52	Farmer	28	No	200 ft.	No	No	Yes	Marked	Posterior
					Status Angina						
J.P.	M	53	Tailor	36	Yes	0	Yes	Yes	No	No	Anterior Posterior
F.C.	M	57	Civil Servant	36	Yes	100 ft.	Yes	Yes	Yes	No	Anterior Posterior
A.C.	M	46	Stevedore	12	Yes	150 ft.	Yes	Yes	Yes	No	Anterior Posterior

away, and 6 cc. of 1 per cent procaine is injected into the pericardial sac. The transversus thoracus muscles are carefully reflected from their attachments on the ribs from the sixth interspace to the third rib. The left internal mammary artery and veins are thus exposed. The artery is freed from the chest wall by doubly ligating the intercostal branches as far away from the artery as possible, from the sixth to the fourth or third intercostal spaces. The internal mammary artery is doubly ligated distal to its sixth intercostal branch, and transected between ligatures. The pericardium is opened, and a traction suture of No. 10 cotton is placed in the heart distal to the point of implant.

A curved pair of mosquito forceps is inserted into the left ventricular wall through a small incision made in the epicardium just proximal to the traction ligature. A tunnel of about 1 inch in the myocardium is thus made. The mosquito forceps emerge from the proximal end of the tunnel to pull the artery into and through the tunnel where it is fixed by traction suture. As the internal mammary artery is pulled into the myocardium, the ligatures on the sixth intercostal and sometimes the fifth intercostal arteries are cut away. These intercostals are bleeding actively at the time of myocardial implant. The pericardium is not closed.

Postoperative care

The most important feature of postoperative care is the maintenance of blood pressure well above 100 mm. Hg. For this purpose, a continuous

TABLE 4
RESULTS

Name	Time since Operation (Months)	Occupation	Angina Pain	Exercise Tolerance		Ability to work—Hours per Day	
				Before	After	Before	After
D.M.	28	Oil field worker	None	150 ft.	1-5 miles	No	8 hrs.
E.S.	28	Executive	Yes	100 ft.	Dances, etc.	No	Part-time
C.A.	27	Machinist	Occasionally, following severe exercise	150 ft.	½ mile	No	16 hrs.
A.M.	21	Grocer	Slight, on severe exertion only	50 ft.	¼ to ½ mile	No	Part-time
S.E.	12	Electrician	None	50 ft.	½ mile	No	8 hrs.
G.A.	3	Farmer	None	200 ft.	Not tested; recent case	No	Too soon
Status Angina							
3 Cases—All died within 62 hours of surgery.							

Neosynephrine drip has been most effective. Likewise, early movement should be avoided until the blood pressure stabilizes.

Pulmonary edema occurs readily. Therefore, not more than 2,000 cc. of fluid per twenty-four hours should be given. Generally, after the third postoperative day these patients present very little trouble, and convalescence is usually uneventful.

Actually, these patients should be considered as patients having had thoracic surgery, who have developed coronary artery occlusion, and be treated accordingly.

Results

The results of operation are shown in table 4. Of the 9 patients, 6 are living and, of these, 5 are well. In the group of 6 cases without angina at rest there have been no deaths. One patient in this group claims he still has

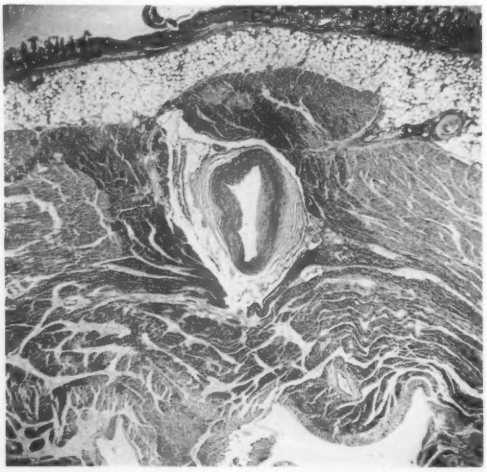

FIG. 11. Section through site of internal mammary artery implant in first human patient operated upon 3 years ago. This patient died 62 hours after implant, quite suddenly, after an uneventful postoperative course. Autopsy showed the only vessel open at time of operation was a pin-point opening in the circumflex branch, which showed a fresh thrombus. Note how internal mammary artery lies between myocardial fibers. There is no hematoma, and the artery itself is widely patent.

his original anginal pain, although his electrocardiogram shows marked improvement. He is able to work part-time. Three are completely free of pain, and 2 experience slight pain in the arm following severe exertion. None could work prior to operation. Now, all except the most recent patient are working—3 of them from eight to sixteen hours daily, and 2 part-time. Exercise tolerance has improved in all; in one case up to 5 miles.

Of the 3 cases of status angina, 2 died sixty and sixty-two hours after operation, and 1 died of cardiac arrest on the operating table. In these patients, the 2 major arteries were found to be blocked at autopsy, and they were living on a pinpoint opening in a remaining vessel. In each instance there was very little muscle left to revascularize, and this was extremely thin.

Figure 11 shows a section through the site of internal mammary artery implant in our first mortality. Note that the artery at the end of sixty-two hours after implantation is widely open, and that there is no surrounding hematoma.

CONCLUSIONS

It has been shown experimentally:

1. That the internal mammary artery after implant into left ventricular myocardium forms anastomosis with left coronary circulation.
2. That the implant is capable of sustaining life and preventing infarction when the anterior descending branch is occluded.
3. That the implant is capable of revascularizing the myocardium in a high percentage of experimental cases.

Nine human cases of coronary artery insufficiency have been subjected to internal mammary artery implantation. Of these, 3 suffered from status angina and all died. In those 6 patients without angina at rest, all were disabled before operation. Three are now working eight to sixteen hours daily, 2 are doing part-time work, and 1 is too recent to evaluate. Three are completely free of pain, and 2 experience only slight pain in the arm after severe exertion. One still has angina.

This work was done in the Department of Experimental Surgery, McGill University, and the Department of Surgery, Royal Victoria Hospital, Montreal, Canada.

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Flat Heads Among the Aged Due to Thin Parietal Bones

J. Gershon-Cohen, M.D., *Harald Schraer,* PH.D., *and Nathan Blumberg,* M.D.

INDIVIDUALS have been found with a curious flat depression of the posterior horizontal portion of the parietal bones due to localized thinness. Epstein recently suggested a relationship between this parietal thinness and postmenopausal, senile or idiopathic osteoporosis.[1] The present report deals with a roentgenographic study of parietal thinness as it was encountered in a group of 130 aged normals, comprising 48 men and 82 women, ranging from 67 to 93 years of age.

RESULTS

X-RAY examination of the skull was part of a complete roentgenographic skeletal survey of each subject. More than two-thirds of these subjects revealed generalized nutritional osteoporosis varying from minimal to moderate in degree; several had marked osteoporosis. Five cases of parietal thinness, an incidence of 3.3 per cent, were found in this group. All of these subjects had moderate skeletal osteoporosis. This compares with an incidence of 0.001 per cent found by the older anatomists and an incidence of 0.46 per cent found by Camp and Nash[2] after a two year roentgenographic study at the Mayo Clinic.

DISCUSSION

WHEN persons with parietal thinness are examined clinically, flattened depressions are palpable in the posterior portion of the parietal bones within 1 inch of the sagittal line. The presence of hair may obscure this thinness which nevertheless may be so marked as to simulate a foramen by palpation. Under such circumstances the condition must be differentiated from congenital parietal foramina. Parietal thinness also has clinical significance when it has to be differentiated from possible areas of malignancy, inflammation, or trauma. This difficulty can be even more pronounced if the thinness is asymmetrical or unilateral.

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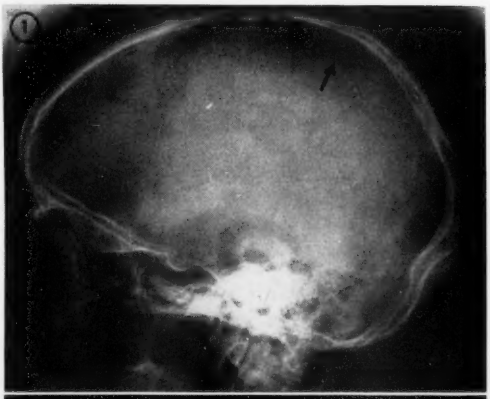

FIG. 1. Thinness of upper posterior portions of the parietal bones. The outer table converges with the inner table producing duplication of projection in the lateral view. The thin area of both parietal bones is radiolucent. This woman, 85 years of age, had moderate skeletal osteoporosis.

FIG. 2. Chamberlain-Towne projection of same skull shown in figure 1, which reveals flat thin area of each parietal bone.

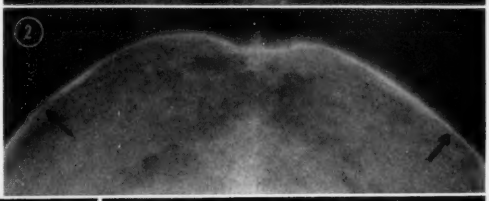

FIG. 3. Parietal foramina in skull from the Hyrtl Collection in the Philadelphia College of Physicians.

FIG. 4. Parietal thinness with artifact foramina revealed by x-ray examination through top of calvarium of another skull in the Mütter Collection, Philadelphia College of Physicians.

The roentgenologist can detect this condition in lateral views of the skull. The localized diploic atrophy and confluence of both tables of the skull can be seen easily. This results in increased radiolucency, a condition which may be

encountered normally and should not serve alone as a basis for diagnosis. Only in the presence of duplicated lines due to the irregularity of the contour of the external table should the diagnosis be made (figure 1). It is important to confirm the diagnosis by anteroposterior projections which must be done with the skull in the proper position for projecting the parietal bones into profile. This is best achieved by variations in the so-called Chamberlain-Towne position (figure 2).

A simple method for determining the degree of osteoporosis by roentgenographic examination is not yet available, but experienced roentgenologists can make estimates that are clinically reliable.

Thinness of the parietal bones has occupied the attention of archeologists, anthropologists, and anatomists for a long time. Among these might be mentioned Virchow, Rokitansky, Broca, Paget, Hutchinson, Keith, and G. Elliot Smith. Whereas these observers of the last century regarded such thinness as a curiosity which might have some anatomical or physiological significance, the modern radiologist no longer associates it with any esoteric process. The best anatomical review of the subject is that by Greig[3] and the fullest roentgenographic report is that by Camp and Nash.[2]

Among the skulls which we examined in the Hyrtl Collection of the Mütter Museum in the Philadelphia College of Physicians, we found an excellent example of parietal foramina and also one of parietal thinness, so marked as to simulate large bilateral foramina (figures 3 and 4).

Greig concluded that parietal thinness was congenital and represented a dysplasia. Some evidence of this possibility was added by Camp and Nash who encountered parietal thinness in the young as well as in the aged. When one considers that the parietal bones are the last to develop and are more subject to changes such as congenital lacunae and trauma, it is not surprising that areas of segmental diploic atrophy with thinning of the parietal bones should occur as variations in ordinary development, simply becoming more prominent in aging atrophic bones. If it is true that parietal thinness is dysplastic, it would follow that some other forms of dysplasia of the parietal bone might result in abnormal thickening rather than thinning. Much to our surprise, we encountered such a case recently. This additional finding makes us more inclined to believe that parietal thinness actually is a form of developmental dysplasia.

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The Treatment of Gout

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RECENT advances in the diagnosis and treatment of gout, together with the resurgence of interest in a variety of articular disorders, have renewed interest in this specific metabolic dyscrasia, which is encountered frequently by both the specialist and general practitioner.

The diagnosis of the acute attack rests upon several criteria. This is a familial disease and in any patient suspected of suffering from gout, inquiry should be made regarding the family history. A positive answer may not be forthcoming at the initial examination but with the passing of time a majority of patients will discover some member of the family to be likewise afflicted. This disease has a high incidence among males, which fact may be of considerable diagnostic help. The age of onset of the first attack varies. In the writers' experience the first attack has appeared as early as the first decade of life or as late as the ninth. If gout is suspected, a review of the past history in regard to previous episodes of undiagnosed acute articular distress may be as helpful as it is in a patient suspected of chronic rheumatic valvular heart disease. The suddenness of onset of acute joint distress is rather typical of gout as it appears in the full intensity within a few hours, usually during the night. Precipitating agents may include direct trauma, a nonarticular infection, dietary indiscretion, emotional distress or the parenteral administration of any one of a number of drugs. In many instances, however, neither the patient nor the physician will be successful in identifying the precipitating agent. The metatarsal-phalangeal articulation of the great toe still is the most susceptible joint although other joints of the feet and ankles, as well as the elbows, knees and wrists, may be affected.

The concentration of serum uric acid is of great diagnostic aid in spite of the fact that the determination of this constituent is fraught with difficulty in many routine biochemical laboratories. If the individual procedure has been expertly performed as determined by past clinical experience, then considerable reliance should be placed upon this determination. Otherwise, the concentration of serum uric acid should not be a determining factor in establishing or excluding a diagnosis of gout. Particular attention should be paid to the administration of uricemic depressants such as cinchophen, salicylates, cortisone, ACTH, and Butazolidin, respectively, during the space of several days prior to the collection of blood for the determination. Each of these drugs may decrease the concentration of serum uric acid with resultant

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equivocal findings. Thus a reliable determination is possible only if the laboratory is qualified from experience to perform such a determination, and if the patient has received no uricosuric agent or serum uric acid depressant for a minimum of three days prior to the collection of blood samples. The finding of subcutaneous tophi and characteristic roentgenographic changes are not to be anticipated in most patients at the time of the first attack of acute gout or during the early years of the disease.

THE RESPONSE to colchicine may be of considerable diagnostic as well as therapeutic value. Hence, there is the dual advantage in treating acute articular distress that is suspected of being gouty in origin with full doses of colchicine as outlined later. Colchicine is a specific for acute gouty arthritis and exerts little or no analgesic action upon other types of articular distress. On the other hand, the several other antirheumatic agents which include salicylates, cinchophen, ACTH, cortisone and Butazolidin as well as opiates may be of therapeutic value but are endowed with no diagnostic implications.

When the diagnosis is established, the therapeutic regimen should be outlined and discussed with the patient. The afflicted person should assume his full share of the responsibility in the day-by-day handling of the malady just as a patient with diabetes mellitus assumes such responsibility. The emotional reactions of the patient should be given early consideration in treatment. An expression of optimism regarding prognosis in a high percentage of cases is justified. If gout is treated properly, few cases become arthritic cripples and the number that becomes incapacitated because of the disease is sufficiently small as to be ignored during the early years of treatment.

The treatment of the acute attack of articular distress involves general as well as specific measures. Colchicine by mouth continues to be the drug of choice. During the past five years other drugs have been reported to be superior but additional clinical experience will be required before we will be willing to recommend the abandonment of oral colchicine as the desideratum for the acute attack. Early administration is a prime requisite. The patient should have colchicine available at all times in order that ingestion of this agent be started with the appearance of the first twinge of pain in the joint. Either the tablet or the granule of colchicine (0.5 or 0.6 mg.) is to be taken orally. Two doses every two hours or 1 dose every hour should be routine until satisfactory subsidence of joint pain is noted or until the onset of gastrointestinal distress. If the attack proves to be a mild one, not more than 4 or 5 tablets are required; gastrointestinal distress is not provoked, and the patient is no more inconvenienced than is necessary to swallow the few tablets. If the attack is moderate or severe, ingestion of colchicine is to be continued without interruption irrespective of the time of day or night until gastrointestinal distress appears. The average requirement for the person of medium weight is 10 tablets. With the development of nausea, vomiting or diarrhea, the ingestion of colchicine should cease and a gastrointestinal sedative given. Tincture of camphorated opium (paregoric) 5 ml. may be

administered and repeated every two hours until the disappearance of these side actions. The subsidence of articular distress usually is prompt. The above description has been identified as a "full course" and is most satisfactory when followed specifically. Optimum benefit from oral colchicine is not achieved if the full course is interrupted. This applies particularly to the fallacy of giving a portion of a full course on one day and finishing at a later time.

Oral administration of colchicine combined with a salicylate or some other antirheumatic drug is not indicated. The use of colchicine intravenously has merit in selected instances. An underlying gastrointestinal disorder may prevent the administration of a full course of colchicine orally or less than a full course of colchicine may have been taken with the development of gastrointestinal intolerance and without the alleviation of joint distress. In either situation, intravenous colchicine (Aqua-colchin*) may be indicated. One of the principal objections to the administration of intravenous colchicine is the belief advanced that a patient should not be dependent upon the immediate availability of a physician for the treatment of acute gouty arthritis such as is required by the intravenous preparation.

In some cases a full course of colchicine does not produce alleviation of joint distress so that a second course of colchicine or some other antirheumatic agent is indicated. Since an interruption of from twenty-four to thirty-six hours is necessary before oral colchicine may be readministered, Butazolidin or ACTH is to be preferred in such situations. Either of these preparations may have a more rapid effect following a course of colchicine than if given initially. The explanation for this phenomenon seems obvious. A full course of colchicine has produced some antiarthritic effect and permits a complementary action for either of these 2 preparations.

Butazolidin† is another effective agent in the treatment of acute gout. This preparation has been received with enthusiasm[1, 2] but our experience as measured in terms of years is limited. The speed of recovery following its administration is more rapid in some instances than that following colchicine; in others it is less rapid. Kuzell[2] notes that complete remission occurred within forty-eight hours with Butazolidin in approximately one-half of his cases. Our experience with colchicine is more favorable. The remainder of Kuzell's patients underwent a slower recovery. Only an occasional patient in our experience fails to experience an adequate remission within forty-eight hours following a full course of colchicine.[3]

Approximately 4 tablets (200 mg. each) of Butazolidin may be taken each day until recovery ensues or this form of therapy is abandoned. As noted previously, there has not been extensive experience with this new drug but selected observations indicate that caution should be exercised when it is used daily in the treatment of other forms of arthritis. The incidence of side reactions is appreciable. Nausea and anorexia, as well as salt

*Aqua-colchin was supplied by Parke, Davis & Company, and †Butazolidin by Geigy Pharmaceuticals.

and water retention, are mildly distressing to the patient but subside with cessation of administration. Stomatitis, cutaneous reactions and bone marrow depression are more serious complications while pulmonary edema and cardiac decompensation are noted more frequently. Butazolidin produces a significant depression in the concentration of serum uric acid and is a mild uricosuric agent. Since the effective treatment of the acute attack of gout is independent of the concentration of uric acid in the serum, these metabolic actions of Butazolidin are not inherent in its beneficial effect. It may be noted that colchicine exerts its full therapeutic effect upon acute joints without a demonstrable effect upon the concentration of uric acid in the serum or upon the excretion of uric acid in the urine. On the other hand, salicylates and cinchophen exert a well established effect upon the depression of uric acid in the serum and an augmented excretion of uric acid in the urine with an incomplete action upon articular distress. Finally, it should be noted that Benemid, a powerful uricosuric agent and depressant of the concentration of uric acid in the serum, is endowed with no immediate antirheumatic action.

THE DRAMATIC subsidence of acute articular distress that has been attributed in selected instances to Butazolidin is reminiscent of the action of ACTH reported a few years ago. Some patients responded rapidly to ACTH; others did not. At this time, four years later, ACTH is believed to occupy a secondary place in the treatment of the acute articular disorder associated with the gouty dyscrasia. One objection to the use of ACTH is the need for a physician or nurse to be available for one or more injections. Obviously, it is neither practical nor desirable to hospitalize patients when other forms of therapy are available which are equally or more satisfactory. Parenteral administration is necessary for ACTH and it has not been shown to be clearly superior in the over-all evaluation of the several antigout preparations. Its principal place is believed to be in the treatment of the occasional attack which does not respond to other forms of therapy. From 50 to 100 mg. of rapid action ACTH should be administered intramuscularly at once if this agent and route are selected. A total of from 100 to 200 mg. of ACTH should be given daily in 2 or 3 divided doses and continued so long as symptoms persist. ACTH-gel, the slower acting preparation, is less desirable because of its inherent delayed effect. If the gel preparation is used, 100 mg. should be administered initially. The most effective means of administering ACTH is intravenously, using 10 to 20 mg. over an eight-hour period. The administration of ACTH may be followed by an exacerbation of acute gout within a week. Wolfson[4] has recommended that this be counteracted by colchicine.

Salicylates or codeine may be taken with each of the above described preparations if an analgesic seems warranted. Neither preparation accelerates recovery but if joint distress is severe, a useful purpose is served. Large doses of opiates at frequent intervals are not to be recommended since this may lead

to confusion regarding the response to the antigout agents. Neither codeine nor morphine is used routinely by the authors in even severe cases of acute gouty arthritis.

The use of cortisone has been associated with less satisfactory results than ACTH in the treatment of acute gout. At times acute gouty arthritis may be relieved; at other times cortisone is not effective in the same patient.

GENERAL measures for the treatment of the moderate or severe attack of gout include rest of the affected joints, abundance of fluids, and a light diet. No useful purpose is served if severely affected joints are subjected to weight bearing or unnecessary motion. If the upper extremities are affected, an arm sling suffices; if the lower extremities are affected, bed rest with a cradle for the bed covers is desirable. Severely affected joints are susceptible to minor cutaneous stimuli, a phenomenon which should be respected. The local application of moist dressings, dry heat, glycerin packs, ice packs, diathermy, ultraviolet radiation and infrared radiation, respectively, have been recommended but are of doubtful value in our opinion.

The systemic reaction to a severe attack of gout is not appreciated fully. A pyrexia of from 2 to 5° F. may be present to confuse the inexperienced physician as well as the patient. Obviously, other causes for a febrile reaction should be excluded but not to the point that the acute gout is overlooked. The pyrexia may be accompanied by chills and a leucocytosis. An abundance of fluids should be insisted upon and serves a dual purpose. Pyrexia is associated with increased fluid loss through the skin and should not be overlooked. Equally important is the need for an adequate amount of fluid for renal transport of uric acid in order to minimize the tendency to precipitation of urates in the renal tubules.

Although the mechanism of acute articular distress in gout is not understood, synovial effusion may be a participating factor, especially in the knee. If an acute attack of arthritis develops in this joint, periodic inspection should be made in order to determine whether or not an effusion of appreciable size is present. If this occurs, the excess fluid should be removed. The physician should have no hesitation in carrying out this procedure under aseptic conditions. An elastic bandage should be applied following removal of the fluid and worn one or two days. If aspiration is not accomplished, the time for recovery of the affected joint may be prolonged. Aspiration is an adjunct to drug therapy and does not replace it; the antigout agent selected should be continued quite independently of this procedure.

Irrespective of the regimen selected for the treatment of the acute attack of gout, the patient should be rehabilitated as rapidly as possible. The patient should be encouraged to move about and to use affected joints as soon as distress subsides. The more rapidly normal function is accomplished, the better the clinical result.

The desirability of the patient appreciating possible precipitating agents should be stressed. Each attack of gout should be documented by the patient in an attempt to allocate an inciting agent if possible. An acute infection,

mild or severe, may prove to be an offending agent. Local physical trauma to a nonarticular area of the body or generalized physical trauma may be followed by acute articular distress. The frequency of a surgical procedure precipitating acute gout has been stressed by Hench.[5] A number of drugs may act as precipitating agents. Thiamine hydrochloride, ergotamine tartrate, liver extract, B_{12}, and insulin are included. Penicillin is worthy of particular note. The diagnosis of pyogenic arthritis may be wrongly presumed when the patient is suffering from acute gout. The temptation to administer penicillin may be doubly harmful. This drug may prolong symptoms in an inadequately treated attack as well as incite other joints to acute activity. Exposure to cold or dampness and overindulgence in food or alcoholic beverages conclude the list of the more common inciting agents.

Considerable emphasis has been placed upon inciting agents because something may be accomplished prophylactically for the patient in this regard. If a precipitating agent is recognized, the gouty patient need not sit back and wait for the inevitable sequence of events to develop. The prophylactic use of colchicine should be regulated according to the occasion. If the patient is on small rations of colchicine daily, the number may be increased for a few days. If he is not on daily rations, this should be accomplished. The prophylactic use of colchicine for two or three days before and two or three days following any surgical procedure should be routine. An acute infection in the gouty patient should be treated by colchicine prophylactically as well as by selected antibiotics if indicated in keeping with conservative medical practice. Prophylactic use of colchicine to permit overindulgence in alcohol or calories is to be condemned.

Persons with a mild form of the disease as well as those more severely afflicted but who respond well to the gouty regimen should be incapacitated by an acute attack at infrequent intervals only. A majority of the total number of patients with gout seen by the respective authors are incapacitated by acute attacks of gouty arthritis on not more than a few days each year. Some patients with a mild form of the malady, irrespective of specific therapy, may experience an attack at less frequent intervals. There are also some patients without benefit of specific therapy who experience frequent attacks of acute gouty arthritis over a period of several years and who subsequently notice a significant diminution in frequency. The "classical" course of the disease that is described, with increasing frequency of attacks and increasing joint involvement, is by no means the inevitable clinical course. The malady is variable and the progression or lack of progression in an individual patient need not follow the characteristic pattern, hence the difficulty of evaluating a specific or a nonspecific regimen in long term management. We are convinced that much may be accomplished by a gouty regimen that is carefully followed. We are equally willing to admit that what appears to be clinical benefit may be a function of the inherent aspect of the disease in a few selected individuals.

Just as colchicine is considered to be the drug of choice in the treatment

of the acute attack, it is also the drug of choice in the intercritical period. Furthermore, just as colchicine has no satisfactory explanation for its pharmacologic action upon acute symptoms, there is no recognized pharmacologic or metabolic action in the intercritical period. The empiric use of the drug, nevertheless, is endowed with great merit. Colchicine has been prescribed by us as a phophylactic agent for almost two decades.[6]

Most patients with gout are advised to take colchicine periodically in the intercritical period.[6] If the affliction is mild and the patient has not more than one attack per year, 1 tablet (0.5 mg.) is recommended three or more days each week. There is only meager evidence that this quantity of colchicine, per se, is of therapeutic value either in allaying minor aches and pains in the gouty joints or in influencing the incidence of acute exacerbations. On the other hand, any patient who has had one attack of acute gout is a potential candidate for subsequent attacks, and if some tablets are ingested each week, a supply is available at such time as articular symptoms return.

Moderately affected individuals should take 1 or more colchicine tablets each day of the year. The severely afflicted should begin with the ingestion of 2 tablets per day and increase to 3 if no gastrointestinal intolerance develops. A few patients may require as many as 4 tablets daily. The precise number in this range should be determined by the gastrointestinal tolerance of the patient as well as by articular benefit.

Intolerance to colchicine during an acute attack of arthritis has not been observed even though the patient has been on periodic prophylactic doses. Patients who have been on daily rations of colchicine for a decade or more receive the optimum benefits from a "full course" when this is prescribed. Another obvious gain from the daily ingestion of colchicine for those moderately or severely afflicted is the advantage in having started a course at an early stage of an attack if acute articular symptoms develop.

Sodium salicylate has been recommended in the treatment of chronic gout because it is analgesic as well as uricosuric. A patient with chronic deforming gouty arthritis may profit from the analgesic effect of salicylates in the intercritical period. From 1 to 2 gm. of sodium salicylate in divided doses may be taken for this purpose. Reliance need not be placed upon salicylates for maximum uricosuric action, however, since Benemid is available.

There are few observations in support of the presumption that cortisone, ACTH, or other steroids are of value in the intercritical period. No clinical experience or documentary evidence suggests that either ACTH or cortisone when administered at frequent intervals reverses metabolic disturbance or reduces incidence of acute attacks of gout.

Regression of osseous tophi has been reported following prolonged salicylate therapy. Two patients reported by Marson[7] ingested from 5 to 7 gm. of salicylate daily and were observed to recalcify osseous tophi as well as sclerose the articular surfaces. A similar observation was recorded by Gutman.[8] We have not observed any improvement of the gouty joint in x-ray films following treatment with salicylates but we have not used doses of

salicylates as great as 7 gm. per day for many months. Salicylism has usually appeared and we have permitted patients to reduce the dosage to not more than 3 gm. per day.

During the past three years a new drug, Benemid*, has been available, which holds great possibilities for its uricosuric action. This action reverts to the observation by Wolfson and coworkers[9] that caronamide (4-carbon-phenyl-methane-sulfonamide) in doses as large as 12 or 15 gm. increased the excretion of uric acid in the urine. Some time later an improved caronamide, Benemid (p-(di-n-propylsulfamyl) benzoic acid) was found to be more effective in much smaller quantities. There is no claim that Benemid is of value in the acute attack of gouty arthritis. Its merit is exclusively in its uricosuric action which occurs concomitantly with depression of uric acid in the serum and depression of the miscible pool of uric acid in the body.[10] The action of Benemid is presumed to reside in the renal tubules where the transport of uric acid occurs. Experimental evidence suggests that uric acid appears in glomerular filtrate in essentially the same concentration as it appears in a protein-free filtrate of serum. Approximately 10 per cent of the uric acid is excreted in bladder urine; the remaining 90 per cent is reabsorbed by the tubules. Any decrease in the percentage resorption of uric acid from glomerular filtrate would result in an increased urine clearance and an increased urinary excretion of this substance. Benemid will lower the blood serum uric acid level by 30 per cent or more, a quality which should help to prevent tophus deposits in the body and to decrease those already present.

Studies conducted several years ago revealed that there were several agents in addition to cinchophen and salicylates that altered materially urate clearance.[11] Intravenous administration of Diodrast (3, 5 diiodo-4-pyridone-N-acetic acid-diethanolamine) is associated with a marked increase in urate clearance. The intravenous administration of hypertonic glucose solution with a hyperglycemia as high as 400 mg. per 100 ml. is associated with a similar outpouring of uric acid in the urine. These were interesting observations in the laboratory but they possessed no practical application. In each instance the uricosuric action was associated with a decrease in resorption of urate by the tubules, an increased urinary excretion of urate, an increased urate clearance, and a decrease in concentration of uric acid in the serum, respectively. Similar changes follow the oral administration of Benemid. Following the ingestion of therapeutic quantities of Benemid, there is an increase in urate clearance as measured by twenty-four hour specimens of 15 or more per cent. The increase in the amount of uric acid excreted may be from 30 to 50 per cent. An increase in urate clearance from two to four-fold following Benemid has been reported by Pascale, Dubin and Hoffman.[12] The action of Benemid upon the urate in the serum and excretion in the urine may be demonstrated within six hours after beginning ingestion.[13]

*Benemid was supplied by Sharp & Dohme, Inc. Benemid is the registered trademark of Merck & Co., Inc., designating its brand of probenecid.

The specific effect upon the exchange of urate in the body may be demonstrated in nongouty controls as well as in gouty subjects. A maximum effect upon the concentration of uric acid in the serum with maintenance doses of 2 gm. per day may be observed within a fortnight after beginning administration. Thereafter the effect in the serum diminishes somewhat but is not abolished and in most patients the uricosuric action may be demonstrated so long as the drug is administered. In our series this duration is more than two and one-half years.

The optimum dosage of Benemid may be determined by the gastrointestinal tolerance of the patient. The daily administration of more than 2 gm. of Benemid for more than a few days is not tolerated by most patients. Only a few patients develop anorexia or urinary disturbances if 2 gm. or less are ingested daily. Many of the gout patients seen by the senior author have been maintained on 2 gm. of Benemid daily throughout the duration of the study. Many patients of the junior author have been maintained on 1 gm. of Benemid daily. The results indicate a slightly greater effect upon uric acid exchange in the former series. Gutman[8] recommends from 1 to 2 gm. a day. Pascale and coworkers[12] report excellent results with only 1 gm. a day. There are believed to be certain theoretical advantages in recommending the larger dose. In patients severely afflicted, larger doses are preferred because of more effective mobilization of periarticular deposits of urates as well as greater inhibition of development of osseous and subcutaneous tophi.

Most patients who are moderately or severely afflicted with gout should be on daily rations of Benemid in addition to colchicine. There may be little justification for recommending Benemid daily to those mildly afflicted unless the serum uric acid level is high. Patients moderately or severely afflicted who have been stabilized rather well on prophylactic colchicine report at least two beneficial effects of Benemid—eventual reduction in the incidence of acute attacks per year and an improved state of well-being. This has been confirmed on a few occasions by stopping Benemid with a return of vague symptoms and resumption of medication subsequently with improvement.

The toxicity of this substance is thought to be unimportant clinically. Apprehension regarding the development of toxic symptoms decreases the longer Benemid is used. The side effects include some slight increase in incidence of acute attacks, increased tendency to passage of uric acid calculi, gastrointestinal irritation, genitourinary irritation, skin rash, and a serious anaphylactic reaction. The only toxic reactions that merit elaboration are the urate calculi and the anaphylactic reaction since the other phenomena subside promptly with cessation of the drug. The incidence of uric acid stones in patients with gout has been noted[11] and should be appreciated before recommending Benemid to any patient with gout. As complete information as possible should be obtained regarding passage of urate sand in the past as well as symptoms suggestive of a urate calculus in the ureter. Some patients with gout report the passage of a urate calculus preceding the first attack of articular distress. In two instances we have proceeded with full knowledge of a positive past history. The incidence of trouble in the series

under study was not enhanced when comparison was made with a similar period before beginning Benemid. Obviously the time is too short to evaluate properly these few data.

Since Benemid leads to a significant increase in uric acid excretion in the urine, every effort should be made to avoid precipitation of urates in the tubules as well as further along the excretory tract. An abundant fluid intake should be stressed irrespective of the administration of this drug. Since the solubility of uric acid in the urine is vital, as large a urine volume as possible should be achieved. The advantage of an alkaline urine in increasing solubility of urate is obvious.[12] From 2 to 3 gm. of sodium bicarbonate may be administered in divided doses as an alkalizing substance. Since salicylates nullify the action of Benemid, these should not be administered concurrently.

The ultimate value of Benemid has not been determined. Recalcification of osseous tophi is objective evidence that is particularly encouraging. Regression in subcutaneous tophi is more difficult to evaluate since a portion of the swelling is caused by nonurate substances and tophi fluctuate in size from time to time without any recognized explanation. It is theoretically possible for large subcutaneous tophi to be resorbed after many months of Benemid intake. Small tophi should regress within shorter periods of time. If Benemid is able to restore the concentration of uric acid in the serum to or toward the normal range, there must be a reverse migration of uric acid from articular and subcutaneous deposits to the miscible pool of uric acid in the body and loss from the body by the way of the kidneys. Since it probably takes years for uric acid to be deposited in macroscopic quantities in and about the joints, a prolonged period is necessary to achieve a reversal. There are no means at present of determining whether uric acid is completely resorbed from tophaceous deposits. Superficial inspection of the joint as well as x-ray examination provides incomplete evidence only. It is possible that with magnified roentgenography more definite conclusions will be possible. Undesirable effects from disruption of the electrolyte equilibrium associated with prolonged therapy have not materialized. The long-term action of Benemid appears to be one of action upon the transport of uric acid and upon no other important phase of metabolic activity.

DIETARY control of the gouty patient in the intercritical period continues to be a subject for disagreement. The total caloric intake should be carefully regulated so that the patient is maintained in a state of optimum nutrition, neither over nor underweight.

The relative content of carbohydrate, protein, and fat furnishes the principal realm for discussion. Avoidance of a high fat diet is indicated clearly. Hubbard and Lockie[14] have shown that a high fat diet may precipitate an acute attack of gout. Furthermore, the incidence of acute attacks is greater on a high fat diet.

The harmful effects of purine foodstuffs have been noted for more than a century. This was based primarily upon the presumption that purines and proteins were the sole precursors of uric acid. Studies in recent years, chiefly

by means of isotopes, have revealed that several relatively simple biologic substances may contribute to the uric acid molecule. These simpler biologic forms include carbon dioxide, formic acid, glycine and lactate. Obviously carbohydrates and fats may be the source of some of these simpler biologic compounds as well as proteins and purines. A diet low in purines but balanced in regard to carbohydrates, proteins and fats is a suitable compromise for the gouty patient if other phases of the gouty regimen are maintained. Furthermore, a better over-all result occurs if proteins are allowed than follows a rigid restriction of proteins as well as purines if colchicine prophylaxis is inadequate and the urinary output insufficient.

Substances high in purines such as liver, kidneys, sweet breads, and anchovies usually can be omitted without hardship. A liberal portion of meat or fowl may provide some additional nucleotides as precursors of uric acid but we believe that the harm is more theoretical than real. With the availability of a powerful uricosuric agent there is less justification for protein restriction than formerly. Purine restriction should be maintained even though Benemid is administered.

An abundant intake of water is highly desirable. Since the concentration of uric acid in body fluids and glomerular filtrate is near the saturation level, the tendency to precipitate urates in the tubules during resorption of fluids, which is greater than the per cent resorption of urate, is a potential threat. Any measure which minimizes this threat is desirable. Tap water should supply most of the ingested fluids daily. Fluids with caloric supplements, such as milk or soft drinks, should be kept at a minimum if there is any need to restrict caloric intake. A high fluid intake in the evening should not be insisted upon if it promotes nocturia.

The harm from a temperate intake of alcoholic beverages is difficult to assess. An occasional patient may prove that a particular beverage acts as an inciting agent for acute gout. On the other hand, most patients with gout are able to remain symptom-free while enjoying a temperate amount of alcoholic beverages if other antigout measures are followed.

Until such time as unsightly tophi are prevented or experience shows that a uricosuric agent will resorb subcutaneous and osseous tophi, surgical interference will comprise one aspect of therapy. The surgical treatment of selected patients with chronic tophaceous gout has been discussed extensively by Linton and Talbott.[15] The feet, hands and elbows comprise the sites that may require surgery. Large subcutaneous tophi which have become unsightly or small tophi of the hands or feet which interfere with wearing of gloves or shoes should be removed. Painful tophi in exposed areas of the body such as about the olecranon bursa, the terminal phalanges of the fingers, toes and heels or the lateral aspects of the feet may be unsightly, painful or the site of a draining sinus. Tendonous involvement by tophi may interfere with motion or locomotion and should be removed surgically.

If the lesion is approached surgically, as complete removal of urates as possible by curettage should be sought. Although extensive tophaceous

deposits eventually may prove to be susceptible to removal medically by a uricosuric agent, a more rapid rehabilitation may be possible by surgical means.

The hazards from surgical interference are negligible. The possibility of postoperative gout appearing necessitates pre and postoperative medication with colchicine as noted previously. Gouty joints are not prone to infection and even before the days of antibiotics, postoperative infection was not a problem. Healing of the incision occurs satisfactorily and patient as well as physician usually is pleased with the results.

SUMMARY

Treatment of the acute attack of gouty arthritis as well as the intercritical period is discussed. Oral colchicine is believed to be the drug of choice for the treatment of the acute attack. Butazolidin and ACTH may be recommended in selected instances. Colchicine is indicated for each patient periodically in the intercritical period. A powerful uricosuric agent such as Benemid may be used together with colchicine but does not replace it. Avoidance of obesity and restriction of purine-containing foods and fats are desirable. A liberal portion of protein daily is permitted. A high fluid intake is stressed. Prognosis is favorable in most patients and an impression of optimism should be conveyed at all times.

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Some of the researches described have been supported in part by grants-in-aid from the Buffalo chapter of the Arthritis and Rheumatism Foundation and from National Institutes of Health, Bethesda.

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Surgical Measures in Hypertension

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THE complications of hypertensive cardiovascular disease probably account for more deaths each year than cancer. A large proportion of deaths and disability from this disorder occurs in persons in the fifth and sixth decades of life. In a small percentage of hypertensive patients (less than 1 per cent) a specific etiological factor can be recognized which is amenable to surgical correction. This small group includes hypertension due to pheochromocytoma, to adrenal cortical adenoma, to unilateral renal disease, to coarctation of the aorta, and that associated with Cushing's disease. This is a tiny but important fraction of the total hypertensive population. Unfortunately, the vast majority of hypertensive patients have essential or malignant hypertension, whose etiology is still unknown, and for which there is as yet no specific therapy. The principal methods of treatment for this variety of hypertension are (1) diets low in sodium or fat, (2) drugs having a hypotensive or sedative effect, (3) surgery in the form of sympathectomy and splanchnicectomy, and (4) combinations of the above three methods.

METHOD OF STUDY

EVERY PATIENT with hypertension must be evaluated thoroughly lest a curable form of hypertension be overlooked, or a patient with severe and progressive cardiovascular disease be denied the benefit of maximum therapy until deterioration into an advanced, irreversible stage of the disorder occurs.

A detailed history and physical examination are essential and should contain data pertinent to the cerebral, cardiac and renal areas.

1. *History*

a. *Cerebral:* paresthesia; weakness and paralysis (transient or lasting); mental confusion; memory loss; headaches (location and type of pain); vascular accident.

b. *Cardiac:* orthopnea; dyspnea; cough; hemoptysis; palpitation; chest pain (type, location and radiation); peripheral edema.

c. *Renal:* eclampsia; toxemia; infection; hematuria; nocturia.

d. *Miscellaneous:* intermittent claudication; abnormal sweating; paroxysmal attacks; fatigue; nervousness; insomnia; epistaxis.

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2. *Physical examination*

a. *Cardiac:* size; rhythm; rate; murmurs; signs of decompensation (gallop rhythm, alternation, rales at bases, engorged neck veins).

b. *Renal:* size of kidneys; masses in renal area (palpate carefully to avoid precipitating a hypertensive attack in pheochromocytoma).

c. *Peripheral vessels:* absence of pulses; evidence of vasospasm.

The eyegrounds should be examined, with fully dilated pupils, by an ophthalmologist. A simple classification has been used which divides the cases into five grades: (0) Normal eyegrounds; (1) Cases with spasm only, generalized narrowing or irregular constrictions, or both, of any degree, without evidence of sclerosis, and without hemorrhage, exudate, or papilledema; (2) Cases with sclerotic changes, particularly arteriovenous compression, generally associated with tortuosity and increased light reflex. Spasm may be present, but hemorrhage, exudate, and papilledema are not present; (3) Cases with hemorrhages and exudate but without papilledema regardless of the changes in the vessels; (4) Papilledema, with measurable elevation of the disk. It is generally associated with hemorrhage and exudate and changes of consequence in the retinal arteries.

3. *Special studies* include the following:

a. If a *cerebral vascular accident* has occurred, such additional studies as skull films, electroencephalograms and lumbar puncture are carried out as indicated.

b. The *cardiac status* is determined by an electrocardiogram and a 7-foot heart plate with particular reference to the size and shape of the heart and the state of the aorta. In patients with significant degrees of tachycardia or those with angina pectoris, Master's two-step test is used to evaluate further the cardiac function.

c. The *renal area* is evaluated by means of urinalyses, a twelve-hour concentration test, and an intravenous phenolsulfonphthalein test, the dye being injected after a period of forced fluid intake, and specimens collected at intervals of fifteen and thirty minutes and one and two hours. This ordinary test of renal function (P.S.P.) has been found useful in estimating the extent of renal damage in hypertensive patients and is the one upon which we have come to rely. A nonprotein nitrogen determination is done and intravenous pyelograms are obtained routinely.

d. *Blood studies* include counts, smears, hemoglobin determination, blood grouping, Rh factor, Hinton, blood sugar, serum protein, Plasma chloride, sodium, potassium, and carbon dioxide content are obtained in certain cases in which a major electrolyte imbalance is suspected.

e. A *postural and cold blood pressure test* is performed as follows: The test is given in both ambulatory and resting states. Ambulatory readings are taken as soon as possible after admission. After at least forty-eight hours of bed rest, except for lavatory privileges, the "resting" test is taken.

Tests are carried out by technicians rather than physicians, since the physician often acts as a pressor stimulus to the patient, thereby causing a higher reading than obtained by the technician. Preliminary readings of blood pressure are taken on each arm. If no great discrepancy exists, the right arm is used. If there is a marked difference between the two sides, this is checked a number of times and the arm with the higher reading is selected. The test is explained to the patient, and after an additional rest period of fifteen to twenty minutes in the horizontal position, observations are begun. It is essential that the environment be quiet, comfortable, and pleasant.

Pulse and blood pressure readings are taken every minute for five minutes with the patient first lying and then standing. With the patient again horizontal, 3 further blood pressure readings are taken at two-minute intervals, then the opposite hand is immersed up to the wrist in ice water (4 to 5° C.) for exactly one minute. Blood pressure readings are taken after thirty seconds and at the end of sixty seconds of stimulation by cold. Readings are continued at two-minute intervals for an additional 3 readings. The patient then assumes the upright position and after 3 preliminary readings at two-minute intervals, the cold stimulus is repeated exactly as in the horizontal position. This is followed by 3 additional readings at two-minute intervals. The average of the first 5 readings in the horizontal position of the first portion of the postural and cold blood pressure test is regarded as the resting blood pressure level.

f. A *sedative test* is performed in all cases. Following a light supper, 3 grains of sodium amytal are given by mouth at 7:00, 8:00 and 9:00 P.M. Hourly readings of pulse and blood pressure are recorded from 7:00 P.M. to 7:00 A.M. The lowest reading of systolic and diastolic blood pressure is taken as the response. This is evaluated by comparison with the average horizontal *resting* blood pressure level as determined by postural and cold test, the diastolic response being the most significant figure.

To be regarded as satisfactory, the diastolic level during the sedative test should fall to 90 mm. or less in patients with resting diastolic levels between 100 and 119 mm. For patients with resting diastolic levels between 120 and 139, sedation response should be a fall to 100 mm. or less. For those with resting diastolic levels of 140 mm. or more, the diastolic level should fall to 110 mm. or less. Otherwise the response to sedation is regarded as unsatisfactory.

g. In cases in whom a *pheochromocytoma* is considered a possible cause of hypertension, a basal metabolic rate and a glucose tolerance test are performed, and a Regitine test is carried out.

HYPERTENSION OF SPECIFIC ETIOLOGY

Pheochromocytoma

Pheochromocytomas are rare tumors of chromaffin tissue which secrete adrenaline or noradrenaline and are most commonly found in the adrenal medulla, but may also occur in other locations outside the adrenal glands. The incidence in our series is about 0.5 per cent.[1] These tumors may cause

paroxysmal or persistent hypertension which at times may be almost impossible to distinguish from essential hypertension. Every effort should be made to establish the diagnosis, since this is a curable form of hypertension. It is distressing to note in the literature that diagnosis of pheochromocytoma has been made chiefly at autopsy (66 per cent). Signs and symptoms characteristic of this tumor should make one suspect the diagnosis. They are excessive sweating, peripheral vasomotor phenomena, elevated body temperature, normal cold-pressor response, fasting blood sugar of 120 mg. per 100 cc. or more, basal metabolic rate of +20 per cent or more, postural tachycardia, postural hypotension, paroxysmal attacks, and glycosuria. Intravenous pyelography may be helpful or even diagnostic. The recent introduction of Regitine as a pharmacologic blocking agent will probably improve diagnostic efforts. We have operated upon 14 patients with pheochromocytoma. There was 1 operative death, this in an elderly patient with a recent subarachnoid hemorrhage. Of the other 13 patients, 12 had lowering of blood pressure levels to normal; 1 had a significant reduction in blood pressure though not to normal. Operative removal of the tumor also usually results in complete reversal of abnormal cardiovascular findings.

Cushing's disease

Most patients with Cushing's disease have an associated hypertension. Following subtotal adrenalectomy, the stigmata of the disease, including hypertension, may be markedly improved. It is not within the scope of this paper to discuss the endocrinologic details of Cushing's disease.

Adrenal cortical adenoma

Yellow adenomas of the adrenal cortex have been found in about 4 per cent of hypertensive patients undergoing splanchnicectomy.[2] These tumors are removed but rarely seem to be responsible for the hypertensive state. In fact we have had only 1 patient whose blood pressure was returned to normal simply by excision of an adrenal cortical adenoma. This is of interest, however, in pointing towards the adrenal cortical hormones as factors in the production and maintenance of human hypertension.

Unilateral renal disease

Although the renal origin of essential hypertension has yet to be proved, there are occasional cases in man which can definitely be attributed to unilateral renal disease. Such disease may be primarily parenchymal or primarily vascular in origin, the vast majority of cases being pyelonephritis. Nephrectomy for unilateral renal disease in hypertension may effect a marked improvement in both blood pressure levels and cardiovascular disease. Only 24 per cent of nephrectomies for hypertension reported in the literature have been successful in this regard.[3] In general, indications for nephrectomy in hypertensive patients should be essentially the same as in nonhypertensive patients. Only seriously affected or nonfunctioning kidneys should be removed, and the function of the remaining kidney should be little if at all impaired. It appears inadvisable to remove the poorer of 2 involved kidneys.

The importance of thorough renal studies in all hypertensive patients cannot be overemphasized. There is a characteristic clinical picture in certain patients with hypertension caused by unilateral renal disease which, if recognized and treated promptly, may result in complete cure: (1) a short history of hypertension, (2) a rapidly progressive and downhill course, (3) severe headaches and retinopathy, (4) a diastolic blood pressure of 130 mm. or more, and (5) a dramatic result obtained by unilateral nephrectomy if instituted early, when the function of the opposite kidney is normal or nearly so.

In our entire series of hypertensive patients we have found only 2 cases in which the hypertension was undoubtedly due to unilateral renal disease, which were relieved by nephrectomy for at least one year after operation. Each patient had an occlusive lesion of one renal artery. One had thrombosis of an aneurysm of the right renal artery, and the other had an arteriosclerotic occlusion of the left renal artery.

SURGICAL TREATMENT FOR ESSENTIAL HYPERTENSION

THE most prevalent form of hypertension is that of unknown etiology—essential or malignant hypertension. The surgical measure which has been found most useful in the management of patients with this disease is splanchnicectomy. We have employed two types of splanchnicectomy: (1) transthoracic sympathectomy and splanchnicectomy and (2) thoracolumbar splanchnicectomy.

Transthoracic sympathectomy and splanchnicectomy. We have used this operation in 7 per cent of surgically treated hypertensive patients. The indications for it are (1) coronary artery disease with angina pectoris, and (2) exertional or postural tachycardia, when associated with hypertension. The sympathetic trunks are removed bilaterally from C3 to D12 inclusive, together with the greater and lesser splanchnic nerves in patients having angina pectoris. For those with unusual tachycardia without angina, the sympathetic trunks are removed from D2 to D12 inclusive.

Thoracolumbar splanchnicectomy (Smithwick operation). We have used this operation in 93 per cent of surgically treated patients with essential or malignant hypertension. The sympathetic trunks are removed from D8 to L1 inclusive, together with the greater and lesser splanchnic nerves. The important effect of any form of treatment for hypertension is its influence on prognosis, as expressed by mortality and survival rates.

DURING the past fifteen years we have studied approximately 3,500 hypertensive patients. Over 2,400 of these have been operated upon and the rest have been treated medically. One thousand, two hundred and sixty-six surgically treated patients and 467 medically treated patients have been followed five years or longer. Patients within the 2 groups have been studied and classified in exactly the same fashion.

The age distribution by decades of the 1,733 patients under discussion is given in table 1. The average age of the entire group when first examined

or operated upon was 43 years. It is to be noted that 69.4 per cent of the group were 40 years of age or older, and that 24 per cent were 50 and over. The age distribution shown in the table does not reflect any intention on our part to exclude older patients from consideration for splanchnicectomy, but is deter-

TABLE 1

AGE DISTRIBUTION OF 1,266 SURGICALLY TREATED AND 467 MEDICALLY TREATED HYPERTENSIVE PATIENTS

Average Age of Entire Group—43 Years

Decades	*No. of patients*	*Per cent*
0-19	17	1.0
20-29	106	6.1
30-39	407	23.5
40-49	787	45.4
50-59	392	22.6
60-69	24	1.4
	1733	100%

mined solely by the age of the patients referred for study. We have tended to be more conservative in offering surgery to persons over 50 but find that in recent years we have been operating upon more elderly patients than in the early years of the study. Patients over 50, or even those over 60, may be benefited as much by surgical treatment as younger patients. To date no relationship between age and results has been demonstrated which contraindicates surgery in the older age group.

All the patients under discussion had *persistent*, not intermittent, hypertension—that is, the diastolic blood pressure in the horizontal position after 48 hours of bed rest in the hospital was 90 mm. Hg. or more. When first seen, the vast majority of these patients had manifest vascular disease in the eyes, heart, kidneys, or brain. They represent, therefore, severe forms of the disorder. This is evident from the survival curves (figure 1) of these patients compared with a survival curve of the normal population of similar age and sex distribution.

Since the prognosis for hypertensive patients varies with the status of the cardiovascular system when first examined, patients with similar degrees

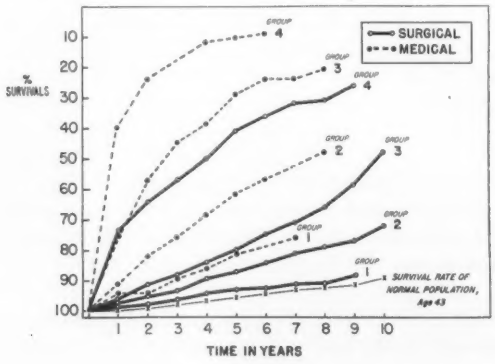

FIG. 1. Survival curves for patients grouped according to Smithwick criteria. These curves have been constructed using the actuarial method. They serve to emphasize the marked differences between the surgical and the non-surgical groups. Although some of the patients have been followed for as long as 14 years, the curves have not been carried beyond the 10-year mark in any case, because either the number of cases is too small to be significant or no further deaths occurred. A survival curve of the normal population is included for comparison.

of hypertension and vascular disease must be placed in comparable groups if there is to be an adequate basis for comparison of results. We have, therefore, adopted a plan designed to control as many of the variable factors as possible. A numerical value is assigned to various factors having a bearing on prognosis. These are summarized in table 2. The numerical values for each factor present are totaled, giving the numerical grade for the patient. Two examples of how to determine the numerical grade are given in table 3. If the numerical

TABLE 2

NUMERICAL VALUE OF VARIOUS FACTORS WHICH INFLUENCE PROGNOSIS

Factors influencing prognosis	*Numerical value of each factor*
Cerebrovascular accident without or with minor residual Abnormal EKG Enlarged heart Impending congestive failure P.S.P.* less than 25% in 15 min., or less than 60% in 2 hr. Age 50 or over Mild angina	1
Cerebrovascular accident, with residual† Frank congestive failure, moderate angina P.S.P.* less than 20% in 15 min. Unsatisfactory response to sedation	2
P.S.P.* less than 15% in 15 min.	3
Nitrogen retention	4

TABLE 3

TWO EXAMPLES OF METHOD FOR DETERMINING NUMERICAL GRADE OF HYPERTENSIVE PATIENTS

Factors considered	*Numerical value*	
Example 1		
Abnormal EKG	1	
Cerebrovascular accident without residual	1	
P.S.P.* 20% in 15 min.	1	
Total	3	= Numerical grade
Example 2		
Abnormal EKG	1	
Enlarged heart	1	
P.S.P.* 10% in 15 min.	3	
Total	5	= Numerical grade

*Phenolsulfonphthalein

†Cerebral deterioration or definite involvement of arm and leg

grade is less than 4, the patient will be in Group 1 or 2. If the numerical grade is 4 or more, the patient will be in Group 3 or 4. The additional factors which determine the exact group of the patient are given in table 4. Patients in both categories, surgical and medical, classified in exactly the same fashion, can therefore be compared with respect to survival and mortality rates within the four groups.

Results of thoracolumbar splanchnicectomy. The five-year mortality rates for 1,266 surgically treated and 467 nonsurgically treated patients are given in table 5. Survival curves for these same patients are shown in figure 1, together with a survival curve of the normal population of the same age.

These survival curves have been constructed using the actuarial method, as described by Berkson and Gage.[4]

From these data it is clear that the mortality rates in all 4 surgical groups are significantly lower than those of corresponding medical groups. This is

TABLE 4

CLASSIFICATION OF HYPERTENSIVE PATIENTS

Group	*Numerical grade*	*Other factors*
1	Less than 4	Eyegrounds grade 0 or 1. No changes in cerebral, cardiac or renal areas.
2	Less than 4	Eyegrounds grade 0 or 1 with changes in cerebral, cardiac and/or renal areas. Eyegrounds grade 2, 3, or 4 with or without changes in cerebral, cardiac or renal areas.
3	4 or more	Resting diastolic level below 140 mm. Changes are present in cerebral, cardiac and/or renal areas but they do not include the following: (a) C.V.A. with marked residual (b) Frank congestive failure (c) P.S.P. below 15% in 15 minutes associated with a poor response to sedation.
4	4 or more	Resting diastolic blood pressure below 140 mm. combined with one or more of the following: (a) C.V.A. with marked residual (b) Frank congestive failure (c) P.S.P. below 15% in 15 minutes combined with a poor response to sedation. Patients with resting diastolic level 140 mm. or more.

TABLE 5

MORTALITY RATES FOR NONSURGICALLY AND SURGICALLY TREATED HYPERTENSIVE PATIENTS

	Nonsurgical series		*Surgical series*	
Group	*No. of cases*	*Mortality at 5 years*	*No. of cases*	*Mortality at 5 years*
1	62	19%	158	8%
2	200	38%	735	13%
3	108	71%	244	20%
4	97	90%	129	59%
Total	467	54%	1266	19%

COMPARATIVE FIVE-YEAR MORTALITY RATES BETWEEN NONSURGICAL AND SURGICAL GROUPS*

Group	*Chi-square*	*p*	*Significance*
1	4.92	.03	Significant
2	60.6	< .001	Highly significant
3	83.2	< .001	Highly significant
4	24.6	< .001	Highly significant

(Yates correction used throughout)

especially so for Groups 2 and 3, where the differences are highly significant. The difference is significant in Group 1, but not highly so. That between the Group 4 cases is also significant, but eventual mortality is still high.

On the basis of our followup data, we can make certain specific recommendations regarding selection of therapy for patients with persistent hypertension. For Group 1 patients, diet and drugs comprise the usual treatment Surgery may be employed in this group for young patients with high resting diastolic blood pressure levels (above 110), for those with intractable symp-

toms, for women with a history of toxemia or other complications of pregnancy associated with hypertension who desire more children, and for those patients who for various reasons are unable to follow a medical regime. For Group 2 and Group 3 patients splanchnicectomy is the treatment of first choice. In Group 4 cases, surgery may be recommended, *provided renal function is adequate.* The one positive contraindication to splanchnicectomy is severe kidney damage as indicated by persistent evidence of nitrogen retention. Although the mortality after surgery is improved, the eventual mortality rate for Group 4 cases is still very high. These patients should not be treated by measures which give little or no benefit until the ideal time for surgical therapy has slipped away. In refractory cases, whether in Groups 2, 3, or 4, diets and drugs may be used with surgery to achieve maximum benefit. Figure 2 shows an example of a 46-year-old Group 3 male patient who has been followed for more than eleven years after splanchnicectomy.

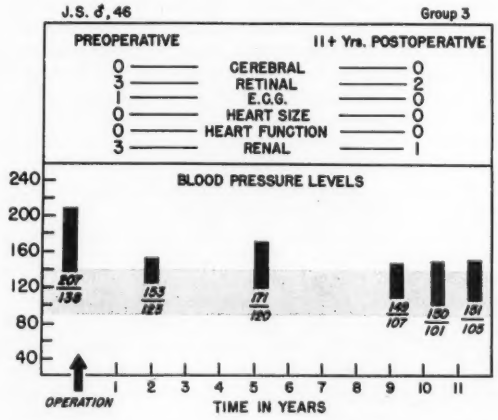

FIG. 2. A 46-year-old Group 3 male hypertensive. Preoperative studies revealed hemorrhages and exudates in his eyegrounds, an abnormal ECG, and impaired renal function. His horizontal resting blood pressure was 207/138. Eleven years postoperative his eyegrounds showed no hemorrhages or exudates, and he had a normal ECG, and improved renal function. His horizontal *ambulatory* blood pressure was 151/105. Blood pressure and cardiovascular status have been significantly improved by splanchnicectomy.

Adrenalectomy. The recent advent of adequate replacement therapy has stimulated renewed interest in the possible use of subtotal or total adrenalectomy for the treatment of essential and malignant hypertension. We are cautiously exploring this matter in certain of our most severe cases. Evidence to date indicates that the most satisfactory results are obtained from a combination of splanchnicectomy and adrenalectomy.[5] Subtotal or total adrenalectomy must be regarded as highly experimental at the present time.

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EDITORIAL

Aging and Health of Men in America

A BASIC HOPE for progress and a constant incentive for research in geriatrics springs from the fact that people age differently. Scientific analysis of this fact is impeded by concentration on a few aberrant individuals or by imputing the differences to the random impact of "outrageous fortune;" the necessity for a statistical approach is clear. But the susceptibility or resistance to aging of a population is not very usefully measured either in terms of numbers of centenarians or of the years of life expectancy from birth. The latter is still mainly dependent on infant mortality, while the attainment of extreme old age in man involves many special questions, both in the ascertainment of facts and in sociological implications.

Thanks to the remarkable progress in control of infective disease and infections, as well as to the less spectacular advances in diagnosis and vital statistics reporting, the statistical position of the causes of major ill health and mortality is increasingly clear. Among adults in America and the Occidental world in general the picture is now overwhelmingly dominated by age-related causes of disability and death so that in an important sense the aging susceptibility of a population, at least in regard to "vital" tissues and organs, is reflected in its mortality rate. Measure the age-specific mortality rate and we have something like a measure of fatal aging versus chronological age.

With these points in mind, it is useful to compare populations for which there are reasonably good vital statistics. The results are revealing, particularly when attention is confined to adults under 70—that is, where ascertainment is best and social significance is greatest. In respect to the mortality rate from all causes, the well-known inferiority of the American male to his wife or sister means, of course, that the sexes must be considered separately. This sex difference, steadily increasing in this country, is often ascribed popularly to the refusal of the female to age rather than to a tendency for the male to age prematurely. Masculine egotism aside, it seems that the American male is not so sturdy, in spite of—or perhaps because of—his massive bulk.

In any case, the American male cannot be fully complacent to discover, for example, that at age 50 his prospect of dying before 60 is considerably greater than that of men of his age in many other countries—17 per cent above Englishmen, 24 per cent above Italians, and 55 per cent above Swedes. These are typical of the results when white men in Europe, the British Commonwealth, and the United States are compared over the age range of 40 to 70 years. In contrast, the durability of the American woman is much closer to that of her sisters elsewhere. The Colonel's lady and Judy O'Grady are alike in more than one way.

There can be little doubt that this relatively premature demise of so many American men is largely or wholly ascribable to "degenerative" disease of the heart and blood vessels—atherosclerosis and its consequences. So far as vital statistics allow detailed analysis, he displays, compared with men elsewhere, no special susceptibility to other major and readily identifiable causes of disability and death — neoplasms, cerebrovascular accidents, nephritis, and hepatic cirrhosis, for example.

This peculiarity of American men obviously merits the closest study, not merely to document more accurately a deplorable state of affairs, but because it would seem there must be lessons in prevention to be learned. Our proclivity to develop early degenerative heart disease has been explained, on dubious grounds, by "tension," though what this is and how it is measured is not specified, by excessive obesity, and by physical indolence. Perhaps all of these play a role, but a strong argument can be made for the importance of the character of the diet. At least when different countries are compared there is a remarkable parallelism between the reported age-specific death rate from heart disease, especially coronary and myocardial disease, and the consumption of total fats in the diet.

The theory that the total fat consumption is involved was suggested by human dietary experiments in which it was found that the concentration of cholesterol and related lipoproteins in the blood serum is strongly influenced by the total fats, both animal and vegetable, in the diet. Explorations on this point, with samples of populations who live on different diets, have recently been made in England, Spain, Italy and South Africa. The results strongly support the theory and add the unexpected information that the effect of dietary fats on the blood cholesterol concentration is absent or trival in young men but becomes increasingly dominant after age 30. Moreover, the evidence suggests that obesity, by itself, is less important than has been suggested by some authorities.

Much more research remains to be done but the clue of blood cholesterol and the diet, and the research tool of studying the experiments of nature with population samples, seems to hold real promise. This is particularly welcome in view of increasing indications that animal experiments in this field have serious limitations because of species differences.

ANCEL KEYS, Ph.D.

(For further details see: Circulation 5: 115, 1952; Lancet 263: 209, 1952; Voed'ng (Amsterdam) 13: 539, 1952; Bull. U. Minnesota Hosp. and Minn. Med. Found. 24: 376, 1953; J. Mt. Sinai Hosp. 20: 118, 1953.)

SOCIOMEDICAL PROGRESS

Devoted to constructive correlation of sociological and medical problems of the aging . . .

Care of the Aged

Norbert O. Hanson, M.D.

IN THE PAST, responsibility for care of the senescent elderly person fell largely upon the shoulders of his children, near relatives, and neighbors. This was particularly true in smaller communities and rural areas. As a form of social security there probably still is none better than a large and happy family. It has been said that if a person has had enough children, even if most of them are blackguards and culprits, there most likely will be at least one among them willing to "take him in" in his old age. Private charities and homes for the aged maintained and supported by various fraternal and church societies provided fine care for limited numbers of elderly people. The county poor farm was the unwanted end of the road for many an indigent and senescent person.

CARE OF THE ELDERLY TODAY

In more recent years, with smaller families, there are fewer to undertake the care of aged parents and relatives. Homes built for the needs of a family of seven to ten children are a thing of the past, and in families otherwise willing and disposed, the limitations of space itself often make difficult the accommodation of an extra elderly person in the home. In large cities and metropolitan areas the problem of care of the elderly created by reason of limitation of space is multiplied even beyond the problem in smaller communities. State hospitals for the mentally infirm become crowded with an influx of elderly senescent persons who might better be cared for in the home or in nearby nursing homes where relatives might be more able to visit them and participate in caring for them.

SENESCENCE

The infirmities and disabilities of the elderly arise from two basic factors. First is the biologic and physiologic evolution and aging of the individual. It begins at birth and proceeds in a more or less orderly fashion. It seems influenced by heredity in that some individuals and families age at more rapid rates than do others, and culminates in tissue changes that have a common denominator in all persons. The selection of one's parents and grandparents undoubtedly has an influence on his longevity. A person is considered old when his hair has become grey, his shoulders stooped, his arteries thickened and hardened, his eyes presbyopic, his hearing impaired, his

NORBERT ORRIN HANSON, *a 1941 graduate of the University of Minnesota Medical School, is consultant in medicine in the division of internal medicine at Mayo Clinic, Rochester.*

skin inelastic with loss of subcutaneous fat, his memory impaired, and his reactions to stress and new situations slowed. Not all these things occur concomitantly in a given individual. Any one of these things may proceed much faster than the others. These symptoms of aging are manifestations of changes in the vascular system, the skeletomuscular system, and the central nervous system. Yet this natural and normal aging is not incompatible with activity of the individual, with self-sufficiency if not a high degree of productivity, and with interest, zest, and appreciation of the joy of living.

This natural process of senescence is of greater concern to the individual, to his family, and to his community when it becomes complicated by certain pathologic conditions. These are the advent of infectious diseases, the development of malignant diseases and new growths, and the misfortune of accident and injury.

Some of these mean only temporary and partial disability, but they may mean prolonged convalescence and more nursing care than can be provided for in the home, yet less than that which demands the occupation of a hospital bed. Unfortunately, all too often they will result in permanent incapacitation and prolonged care until the end. Nursing homes offer an excellent means for providing care under these circumstances.

People in nursing homes might be divided into three categories: those who are ambulatory, those who are disabled but capable of limited activity with assistance, and those who are bedfast. With respect to their mental faculties they might be classified as alert, apathetic, or disoriented. Frankly disoriented and psychotic persons are difficult to care for in nursing homes and disrupt the care of others. Usually they can be better and more properly cared for in mental institutions. Those who are ambulatory and alert may be able frequently to care for their own physical needs, feed themselves if proper nutritious food is available to them, and assist, capably and gladly, in the care of the less active and more feeble ones in their small community. The person who is partially disabled, for example, with partial paralysis as the result of a stroke, may be unable to be up and about, yet may be fully aware of his surroundings, interested in the activities about him, and receptive to participation in his own care. Bedfast persons require most careful attention and thoughtful anticipation of the problems with which they are likely to be faced.

PROLONGED CARE

The person confined to bed is subject to formation of bedsores, loss of appetite, difficulty with elimination, development of pulmonary and urinary complications, and development of apathy, introspection, and depression. The prevention of decubitus ulcers, always a difficult problem, is best met by maintenance of an optimal state of nutrition. The patient is encouraged to take an adequate amount of protein in particular, as well as adequate amounts of carbohydrates, fat, vitamins, and mineral-containing foods. If necessary, regular meals are supplemented with lunches taken between meals. Frequent changes of position to avoid prolonged pressure on any one part and the use of rubber rings or, better yet, sponge rubber at points of pressure are important. Getting the person to sit up in a chair whenever possible is also helpful. Changes of posture will help also to prevent development of pulmonary infections.

As much activity of the extremities as possible should be maintained in order to help preserve muscle tone and the range of motion in joints which otherwise may soon become stiff through disuse. Maintenance of an adequate intake of fluid so that the urinary excretion approximates at least one quart a day will usually suffice for satisfactory renal excretion. Proper bowel habits and the prevention of constipation are important. Activity in so far as it is possible is helpful, and it seems

wise to keep the use of cathartics to a minimum except for persons who have long-established habits with respect to the use of them. Use of a bedside commode in place of the time-honored and despised bedpan has its advantages.

Pulmonary infections and common infections of the urinary tract usually require the help of a physician. Physicians now have at their command chemotherapeutic and antibiotic drugs which will control the great majority of bacterial infections.

Much can be done for the failing heart. It can be benefited by proper medication on the advice of a physician and by avoidance of an excess of salt in the diet (a field for ingenuity on the part of the nursing attendant and cook). Moderate physical activity within the limits of the individual concerned should be encouraged. Heart disease need not mean complete invalidism by any means.

RECREATION AND HOBBIES

All who have given thought to the care of the aged are impressed with the need for recreational interests to maintain active and stimulated minds. Abrupt retirement by virtue of reaching some predetermined age, or that occasioned by the sudden onset of disease, holds for most persons terrors of inactivity. Those who find it easiest to adjust to such changes are those who have maintained activities apart from their occupations, who have found stimulation in hobbies, and who have had interests that carry them away from themselves and give them avenues for thought apart from introspection and reflection on their personal sad state of affairs. In the small community of the nursing home, there are outstanding opportunities for the development of interests, the encouragement of hobbies, and the introduction of group-participation activities.

Hobbies fall into four groups. The first are the creative hobbies. Familiar to all are knitting, needlework, and crocheting, all of which our grandmothers did. Simple things like whittling, wood carving, and making one's own corncob pipe were all hobbies of men. Painting, basketry, sculpture, carpentry, gardening, and the raising of flowers are also creative hobbies. The possibilities are innumerable.

Then there are collecting hobbies. Common ones are stamp collecting and coin collecting. Usually these begin in early life and are a lifelong hobby for those who participate in them.

The third category of hobbies is the educational one, that is, those concerned with the acquisition of further knowledge. Books and reading offer avenues for endless hours of pleasure to those who find them interesting. They demand only a good pair of eyes or an attentive pair of ears if a reader can be found. Public library facilities are within the range of many.

The fourth category of hobbies involves participation. Participation in observation of sports, in community singing (if necessary, only as a listener if one has a disagreeable voice), in card games, or in discussion groups, or even interest in radio programs or television or recorded music is helpful. Activity of the mind is a sign of youth. Just as a tool becomes rusty and useless through disuse, an unstimulated mind and a body not used with care and discretion soon degenerate.

In conclusion one might quote the whimsical, wistful statement of the late British wit, George Bernard Shaw, who lived to a ripe old age: "Youth—," he said, "such a wonderful thing! What a pity to waste it on young people."

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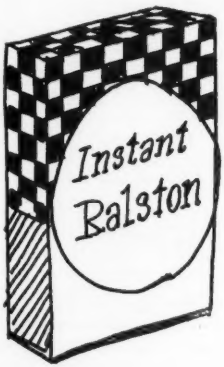

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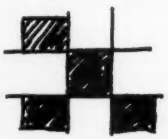

GERIATRICS *Book Reviews*

Surgery of the Pancreas

Richard B. Cattell, M.D., and Kenneth W. Warren, M.D., 1953. Philadelphia: W. B. Saunders Company. 374 pages, $10.00.

This is a splendid book based on experiences with over 1,000 patients with surgical diseases of the pancreas treated at the Lahey Clinic. As Dr. Lahey states in the foreword, this book is a fine example of what a man can do when he can limit his field of interest and then can get his hands into an enormous amount of material in his field. Obviously such material can be obtained only in large clinics.

Every good physician knows that in the last 20 years interest in the pancreas has been increasing, and as a result more diagnoses of pancreatic disease are being made. More efforts are being made to cure persons with severe diseases of the pancreas, even cancer. The book is well written and nicely illustrated, and covers the subject very well.

In regard to chronic relapsing pancreatitis, Cattell says that in the majority of cases surgical measures will be required to control the symptoms. Actually there are many operations that are done. Some are on the biliary tract; others are designed to shunt food out of the upper part of the duodenum; cysts may be drained, stones can be removed, and parts of the pancreas resected, and when there is much pain nerves can be cut. Dr. Cattell is to be congratulated on a fine piece of work.

WALTER C. ALVAREZ, M.D.

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The Physiological Bases of Gynecology and Obstetrics

S. R. M. Reynolds. 1952. Springfield, Illinois: Charles C. Thomas, Publisher. 153 pages, $5.50.

This monograph of 151 pages is divided into 15 chapters which are the no doubt somewhat condensed lectures presented by the author in Montevideo, Uruguay. They represent in large part the results of the author's own work on the various aspects of the physiology of the pregnant uterus. In addition, consideration is given to some aspects of the function of the ovary and particularly the relation of this to its blood supply. One chapter deals with fetal maturity.

It is impossible to review in detail a work which covers such a wide field. The author is the senior worker in this field and, as such, the book carries his authority. It is in a sense a condensed form of his book, *The Physiology of the Uterus*, with stress on the practical aspects of his experimental work. He has the delightful ability of making this material readable and readily understandable. What is at least as important, he is able to stimulate the reader's curiosity.

This is a book which should be read by all who are working in the field of obstetrics and gynecology if they do not have the time to master the larger book. It is relatively new work with wide practical application.

The book is a volume of the American Lecture Series. It is printed on plain paper without illustrations. There are only occasional proofreader's lapses.

JOHN L. MCKELVEY, M.D.
Department of Obstetrics and Gynecology, University of Minnesota

•

The English Pioneers of Anaesthesia

F. F. Cartwright, 1952. London: Simpkin Marshall, Ltd. Baltimore: Williams and Wilkins Co. 338 pages, $4.50.

This book will be a delight to all students of medical history and particularly those interested in anesthesia. It represents a great deal of research and is full of copies of letters from Humphrey Davy, Thomas Beddoes, Hickman and others. Humphrey Davy and Dr. Beddoes became so interested in the results of breathing the several gases then new, gases such as oxygen, carbon dioxide, nitrogen, nitrous oxide, and hydrogen, that they experimented on themselves and studied the effects on small animals. They opened in London a Pneumatic Medical Institution, a clinic in which for several years people were treated with gases. Because it was observed that the breathing of oxygen helped persons who were short of breath, it was hoped that the gases might cure tuberculosis and also paralysis.

At first the institution was successful and patients attracted by high hopes flocked in, but soon they discovered that no miracles were being performed. The only persons who were spectacularly cured for a while were those with hysterical troubles.

About 1798 Humphrey Davy started inhaling nitrous oxide. He and his friends left detailed descriptions of their sensations, and once Davy wrote about the ability of the gas to destroy physical pain. Because of this he felt it might be used in operations. Unfortunately he does not appear to have induced any surgeon to try out his idea.

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The person who came nearest to discovering anesthesia, back in 1828, was Henry Hill Hickman. He found he could produce insensibility by excluding atmospheric air or by giving carbonic acid gas. He definitely intended to use the procedure for surgical anesthesia. Unfortunately he died when he was 30. He recorded an experiment in which he filled a glass globe with the gases exhaled from his own lungs. Into the globe he put a kitten, which became so unconscious that Hickman could cut off its ears and tail without waking it.

WALTER C. ALVAREZ, M.D.

•

Roentgen Examinations in Acute Abdominal Diseases

J. Frimann-Dahl, M.D., Ph.D., 1951. Springfield, Illinois: Charles C. Thomas, Publisher. 312 pages, 357 illustrations.

This is an excellently written book presented in an authoritative manner. Dr. Frimann-Dahl goes into the pathologic physiology of the gastrointestinal tract to explain the many phenomena which help to make the diagnosis in the "acute abdomen." By this method the reader will undoubtedly retain more of the knowledge presented. The author presents details on technic which are not usually used. The cooperation of the surgeon and the roentgenologist is stressed.

The common practice in Norway of screening all chests by fluoroscopy is mentioned. In the United States the large 14x17-inch chest film is substituted and while there are advantages to fluoroscopy, I believe the greater detail obtained on the film is much more desirable. Intestinal obstruction is discussed in great detail. The relationship to duration of symptoms and expected findings are discussed.

The roentgen investigation discussed is based principally on an examination without contrast media. Positions not normally used in our initial examinations are explained by Dr. Frimann-Dahl. It would be well to absorb some of this material so that we may also include them in our armamentarium. He also mentions the need for supplementary examination such as the barium enema or a small amount of barium by mouth when indicated.

The importance of making an accurate and early diagnosis in the acute abdomen is recognized by everyone. Dr. Frimann-Dahl does an excellent job presenting his knowledge and experience to the medical profession. The reproductions and illustrations are excellent and easily understood. The book should be reread several times in order to absorb many of the details set forth.

LEO BLANK, M.D.,
Department of Radiology, University of Minnesota

GERIATRICS *in the* NEWS

All announcements and news relating to geriatric medicine and research should be directed to GERIATRICS, Editorial Department, 84 South Tenth Street, Minneapolis 2, Minnesota.

Blakeslee Award

Entries are being received for the second annual **Howard W. Blakeslee Award** of $1,000 for outstanding scientific reporting in the field of diseases of the heart and blood vessels. The award is presented by the American Heart Association to the individual whose creative efforts in any medium of mass communication are judged to have contributed most to public understanding of heart and circulatory diseases. Entries must be submitted by January 15, 1954. Additional information may be obtained from the award committee of the American Heart Association, 44 East 23rd Street, New York City.

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Kellogg Foundation Grant for Colorado Study

A three-year grant from the Kellogg Foundation has been made to the Colorado Department of Public Health for study and research into community services and facilities for the chronically ill, aged, and aged sick. Dr. Ruth Howard, former public health staff director of the department, will direct the project.

■

New Publications

Section 2 of a study on **Standards of Care for Older People in Institutions,** subtitled "Methods of Establishing and Maintaining Standards in Homes for the Aged and Nursing Homes," has just been published by the National Committee on the Aging of the National Social Welfare Assembly. It is available at $1.00 a single copy from the National Social Welfare Assembly, 345 E. 46th Street, New York City, with special rates for larger quantities.

Old Age in Rhode Island, a report of the Governor's Commission to Study Problems of the Aged, presents the findings and conclusions resulting from their study, together with an outline of a coordinated state program for improving the welfare of the aged. Requests for copies may be sent to the commission at 24 Mason Street, Providence, R. I.

Announcing

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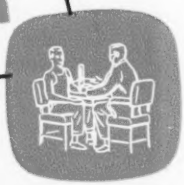

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The inherent dangers of hexamethonium (though greatly reduced because of lower dosage required) call for the same caution, the same diligent supervision, the same careful instruction of the patient, which hexamethonium always demands.

Though the mild hypotensive effect of Rauwiloid is realized slowly, it does not impede the speedy action of hexamethonium.

Associated symptoms of severe hypertension rapidly yield to the Rauwiloid component; tachycardia is relieved by mild bradycardic influence, and gentle sedation changes the usually present anxiety to a feeling of tranquility and well-being.

The concept that it may be "better medicine" to give such potent drugs as hexamethonium individually, and not in combination, does not apply here. Unfortunate mistakes in dosage taken by the patient are less apt to occur when only one tablet-medication has to be taken.

Only the contained hexamethonium need be considered for dosage purposes. Increasing the dosage of Rauwiloid beyond the minimum effective dose will neither lead to excessive hypotensive, bradycardic, or sedative effects, nor produce side actions.

Evidence indicates hexamethonium dosage should be raised slowly. Here is a safe rate of build-up—a uniform, slow, safe rate—with this combination:

Initiate therapy with ½ tablet (each scored tablet contains Rauwiloid 1 mg. and hexamethonium 250 mg.) q.i.d., not less than 4 hours apart, preferably before meals and on retiring. After two weeks, if needed, dosage may be increased by one tablet per day, but not oftener than twice weekly.

Write today for your copy of the new brochure "Rauwiloid+Hexamethonium in the Treatment of Severe, Intractable Hypertension"; it presents a careful review of warning signs in the use of hexamethonium and of the simplification of management made possible by this combination.

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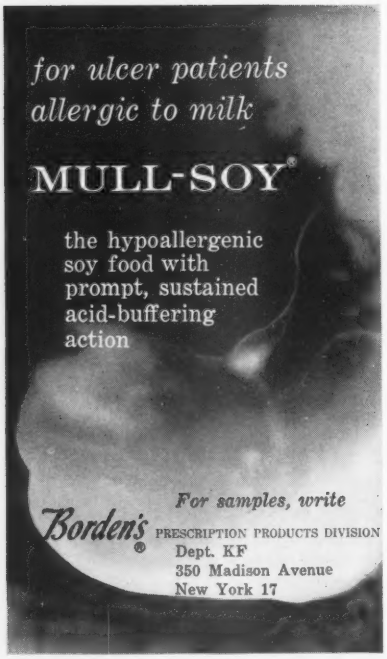


reinforced action
in common infections

Erythro-sulfa*

antibiotic action of erythromycin
chemotherapeutic
effect of triple sulfonamides

valuable especially in staphylococcal, streptococcal, and pneumococcal infections

Each tablet contains

Erythromycin	100 mg.
Sulfadiazine	0.083 Gm.
Sulfamerazine	0.083 Gm.
Sulfamethazine	0.083 Gm.

*TRADEMARK

Upjohn

THE UPJOHN COMPANY, KALAMAZOO, MICHIGAN

NEWS *from Advertisers*

New Percorten Dosage Form

Percorten trimethylacetate (desoxycorticosterone trimethylacetate Ciba), an intramuscular repository for protracted therapeutic effects in adrenocortical insufficiency, has been released to the medical profession by Ciba Pharmaceutical Products, Inc., of Summit, New Jersey.

The advantage of this new dosage form of desoxycorticosterone is exemplified in patients with Addison's disease. Heretofore, such individuals required therapy more or less constantly. With this new Ciba preparation, following stabilization of the patient, a single injection per month is sufficient to maintain the patient on an ambulatory basis. This long-acting steroid hormone derivative provides a constant supply of the hormone at a level required for optimal maintenance of the patient.

This protracted and constant therapeutic effect is achieved because the suspension, when administered by deep intramuscular injection, "behaves like a miniature pellet in that a small fraction of the total dose is absorbed daily." Patients who have Addison's disease and who are not in crisis can now be treated on a practically ideal ambulatory basis. •

New Type of Product for Obesity

The first preparation for metabolic control of obesity, protecting the already-damaged liver of the overweight person, has been made available to the medical profession by Lakeside Laboratories, Milwaukee, Wisconsin.

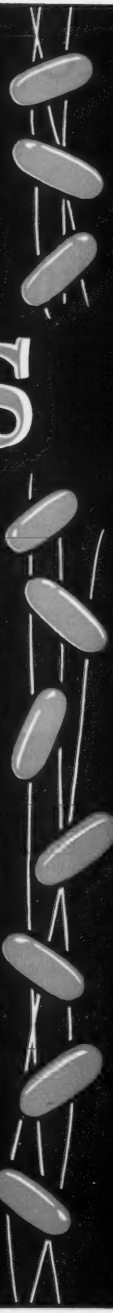
Called Obelip, the product contains important lipotropics which aid and protect the liver by curbing fatty deposition and mobilizing depot fat for metabolic burning. Published evidence has shown that in no case of obesity has the liver been entirely normal.

Obelip is indicated for comprehensive treatment of obesity as it contains appetite regulators in addition to the lipotropic agents choline bitartrate (400 mg.), d-methonin (150 mg.), and Vitamin B12 (4 mcg.). The regulators are d-amphetamine sulfate (5 mg.) to help depress the appetite and to elevate the mood; phenobarbital (16 mg.) to ease tension and avoid jitteriness, sleeplessness and compulsive

a suitable choice for lipotropic therapy in

CIRRHOSIS • CORONARY DISEASE
ATHEROSCLEROSIS • DIABETES

GERICAPS



Gratifying clinical improvement reported with the use of lipotropics in cirrhosis, coronary disease, atherosclerosis and diabetes has resulted in widespread adoption of this therapy.

The choice of the lipotropic used is critical to the patient's response and the success of this management. Gericaps offers a high potency lipotropic formula plus *extra* factors to assure optimal results.

Each Capsule Supplies:

- CHOLINE & INOSITOL synergistically equivalent to aproximately 1 Gm. of choline dihydrogen citrate. Superior potency of the *true* lipotropic factors.
- RUTIN 20 mg. and VITAMIN C 12.5 mg. To help prevent or improve capillary fragility and/or permeability.
- VITAMIN A 1000 units and B-COMPLEX 7.25 mg. To aid in compensating for deficiencies in a fat and cholesterol restricted diet.

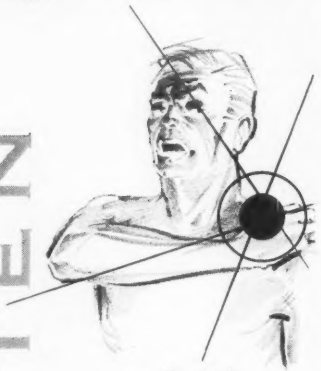
Supplied in bottles of 100

SHERMAN LABORATORIES
BIOLOGICALS • PHARMACEUTICALS
WINDSOR DETROIT 15, MICH. LOS ANGELES

NEOCYTEN

Trademark

Analgesic · Muscle-Relaxant



NEOCYTEN

to abolish the pain-spasm cycle

in neuromuscular disorders

In each NEOCYTEN* *Entab*:

For Potentiated Analgesia

Sodium Salicylate . 0.25 Gm.
Para-Aminobenzoic Acid ..... 0.25 Gm.
Ascorbic Acid ... 20.0 mg.

For Safer Cholinergic Action

Physostigmine Salicylate..... 0.25 mg.
Homatropine Methylbromide . 0.50 mg.

SUPPLIED:
Bottles of 200, 500, and 1000 *Entabs* (enteric-coated tablets).

Samples and literature available to physicians on request

THE CENTRAL PHARMACAL CO.
Products Born of Continuous Research
SEYMOUR, INDIANA

*Trademark of The Central Pharmacal Co.

eating; and methyl cellulose (160 mg.) to eliminate bulk hunger and still hunger contractions.

Duotinic Capsules

Ives-Cameron Company, Inc., New York City, announces the national release of Duotinic capsules—the non-constipating hematinic with the "dove-tailed" formula, containing all known essentials for the rapid regeneration of hemoglobin and red blood corpuscles. Duotinic capsules are indicated in the treatment of most of the commonly encountered anemias of the hypochromic microcytic or hyperchromic macrocytic type. The special advantage of Duotinic capsules consists of notable freedom from "iron-constipation" achieved by the inclusion of extract of hog bile (desiccated) in a carefully adjusted dosage to avoid purgation. The desiccated extract of hog bile also improves iron absorption particularly in biliary dysfunctions.

Each Duotinic capsule contains: ferrous sulfate (exsicc.) 200 mg., Vitamin B_{12} U.S.P. 10 mcg., folic acid 375 mg., ascorbic acid 50 mg., extract hog bile (desiccated) 100 mg., whole stomach substance 100 mg., desiccated liver NF 100 mg.

reinforced action in common infections

Ery|thro|sulfa*

antibiotic action of erythromycin
chemotherapeutic effect of triple sulfonamides

valuable especially in staphylococcal, streptococcal, and pneumococcal infections

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Erythromycin . . . 100 mg.
Sulfadiazine . . . 0.083 Gm.
Sulfamerazine . . 0.083 Gm.
Sulfamethazine . 0.083 Gm.

*TRADEMARK

Upjohn

THE UPJOHN COMPANY, KALAMAZOO, MICHIGAN

Meat...

and the Important Role of Protein in Hemoglobin Synthesis

Although the relationship between iron and hemoglobin formation is widely appreciated, the important role played by protein in hemoglobin synthesis is relatively obscure. Nevertheless, since globin is just as much a component of the hemoglobin molecule as is iron, the continued synthesis of this protein is necessary for normal hemoglobin production.

It has recently been estimated that in the average adult 8 Gm. of globin is destroyed daily.[1] This means "that approximately 14% of the total dietary protein intake of the average adult [female] is required solely for the re-synthesis of new hemoglobin. These data reemphasize the importance of adequate protein, as well as iron, intake for the maintenance of a normal rate of hemoglobin synthesis in man."[2]

Because meat is an outstanding source of *both* iron and high quality protein, it is always recommended in generous amounts in the dietary management of hypochromic anemia. These nutritional values, as well as its significant content of B vitamins, also make meat an important component of the daily diet of normal persons.

---

1. Drabkin, D. L.: Metabolism of Hemin Chromoproteins, Physiol. Rev. *31*:345 (1951).
2. The Biosynthesis of Hemoglobin, Editorials, J.A.M.A. *150*:1223 (Nov. 22) 1952.

The Seal of Acceptance denotes that the nutritional statements regarding meat made in this advertisement are acceptable to the Council on Foods and Nutrition of the American Medical Association.

American Meat Institute
Main Office, Chicago...Members Throughout the United States

NOTES: CONSTIPATION

WHAT BULK-PRODUCING PRODUCT IS EFFECTIVE FOR BOTH SIMPLE AND INTRACTABLE CASES?

Simple constipation

Many physicians report excellent results in the treatment of ordinary constipation with Hydrocil. Hydrocil absorbs liquids with unusual efficiency, creating 35 times its own weight of moist, lubricating bulk. Patients find Hydrocil pleasant and easy to take, too.

Intractable constipation

When mild bowel stimulation is desired in addition to effective bulk therapy, Hydrocil Fortified is recommended. To supplement its bulk-producing ingredients, Hydrocil Fortified contains acetphenolisatin, a newly-developed synthesis of the laxative principle in prunes.

This gentle, persuasive laxative has proved highly successful in correcting intractable constipation and preventing impactions after anorectal surgery.

How supplied

Hydrocil Fortified (blue label) and Hydrocil Regular (brown label) are provided in 4-oz. and 1-lb. canisters. A supply of Hydrocil for trial will be sent you upon written request. Address: Dept. G-5, Fuller Pharmaceutical Company, 715 So. 10th St., Minneapolis 4, Minn.

Hydrocil *Fortified • Hydrocil Regular • Benadex Benzocones • Tucks • products of...*

fuller PHARMACEUTICAL COMPANY

Upjohn

cortisone for inflammation, neomycin for infection:

Each gram contains:

Cortisone Acetate . . . . . 15 mg.

Neomycin Sulfate . . . . . 5 mg.
(equivalent to 3.5 mg. neomycin base)

Available in 1 drachm tubes with applicator tip

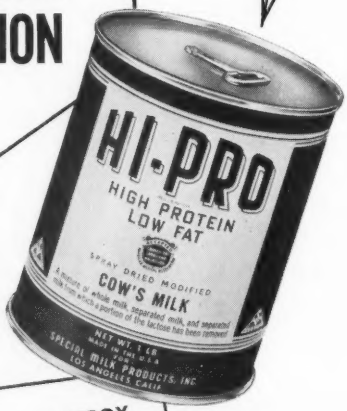
The Upjohn Company, Kalamazoo, Michigan

Neosone

Trademark

OPHTHALMIC OINTMENT

Points the Way to Economical-Palatable WHOLE PROTEIN SUPPLEMENTATION



A specially prepared, spray dried modified cow's milk, which mixes readily with water, milk or other beverages and foods. It may also be incorporated into desserts, cereals, batters, etc. HI-PRO tastes so good patients enjoy taking it.

Suggested Recipes

CONTENTS:	SUPPLIES:	APPROX. COST:
HI-PRO – 3 oz. Whole Milk – 8 oz.	Protein – 44 gm. Calcium – 1.4 gm. Calories – 550	34¢
HI-PRO – 8 oz. Water – 1 pt.	Protein – 98 gm. Calcium – 2.8 gm. Calories – 1000	75¢
HI-PRO – 1 oz. in Food of Choice	Protein – 12 gm. Calcium – .35 gm. Calories – 121	9¢

Available at all pharmacies in 1 lb. vacuum tins.

HI-PRO

Send for Samples and Documented Booklet on HI-PRO... its uses in adult therapy.

Jackson-Mitchell Pharmaceuticals, Inc.
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• CULVER CITY • CALIFORNIA • SINCE 1934 •
PRODUCTS

Gantrisin 'Roche' — a single, soluble, wide-spectrum sulfonamide —

Gantrisin 'Roche' is especially soluble at the pH of the kidneys. That's why it is so well tolerated... does not cause renal blocking... does not require alkalies. Produces high plasma as well as high urine levels. Over 150 references to Gantrisin® in recent literature.

A new, potent antibacterial—

Gantricillin-300 Roche

... for wide-spectrum antibacterial therapy. Each Gantricillin®-300 tablet provides 300,000 units of penicillin PLUS 0.5 Gm of Gantrisin®--the single, soluble sulfonamide.

When Chronic Fatigue, Insomnia are due to Low Blood Sugar Level . . .

Prescribing a simple change in diet may often restore energy and zest for living in many patients.

THE pace of modern living . . . business pressures, strenuous social activities, hurried meals, improper diet . . . all too frequently lead to exhaustion, loss of energy, inability to sleep. Now clinical studies show that these clinical manifestations are often associated with hyperinsulinism—causing a lowered *blood sugar level.**

Portis reported these fatigue states were aggravated when the patients consumed beverages and foods that contained free sugar. He further stated that while these raise the blood sugar level momentarily, their "free" sugar is burned up too quickly, and a greater letdown follows. On the basis of this evidence a diet high in proteins and relatively high in carbohydrates in a complex form was given to his patients. He found such foods as milk are especially beneficial because they are digested more slowly, and because they maintained the blood sugar level for a longer period.

For these reasons milk with Postum is suggested as a between-meal feeding and bedtime drink. It can often be of practical benefit to the patient. The milk provides nourishment that is slowly, steadily converted to blood sugar. Postum offers a pleasant and palatable flavor. Postum offsets the distaste for hot milk.

Moreover, Postum in the milk drink has a psychological advantage because many patients resent the taking of milk in itself as a regression to their childhood patterns. Postum has been recommended by doctors for over 40 years. It is widely known to your patients as a caffein-free drink—a beverage that has helped countless caffein-susceptibles to break the coffee and tea habit.

We will be glad to secure for you a reprint of Dr. Portis' article. We will also send you without charge a supply of Postum for your patients if you send in the coupon below.

*Portis, Sidney A., Life Situations, Emotions and Hyperinsulinism, J.A.M.A. **142:** 1281-1286 (April 22) 1950.

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A Product of General Foods

Postum, Dept. G-11, Battle Creek, Mich.

☐ Please send me without charge or obligation reprints of Blood Sugar Studies published in the A.M.A. Journal.

☐ Please send me a Professional Pack of POSTUM containing 12 sample-size packages.

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Offer expires Dec. 31, 1951. Good only in Continental U. S. A.

OPPORTUNITY

Well-established hospital and clinic with 12-person professional staff, approved by and members of A. M. A., A. C. S., A. H. A., state hospital association and other bodies, seeks *a doctor with some special training and interest in geriatrics.*

County seat town of 14,000 in southern plains of Texas panhandle. Federal highway and Santa Fe Ry. serve community and adjacent agricultural area. Educational, cultural, recreational facilities. Solid citizenry; prosperous, civic-minded. A guarantee of $1,000 per month and 50% of the collectible. Write Box 931, c/o Geriatrics.

reinforced action in common infections

Erythro-sulfa*

antibiotic action of erythromycin
chemotherapeutic
effect of triple sulfonamides

valuable especially in staphylococcal, streptococcal, and pneumococcal infections

Each tablet contains

Erythromycin . . . 100 mg.
Sulfadiazine . . . 0.083 Gm.
Sulfamerazine . . 0.083 Gm.
Sulfamethazine . 0.083 Gm.

Upjohn

*TRADEMARK

THE UPJOHN COMPANY, KALAMAZOO, MICHIGAN

Your Patients Can Break Laxative Habit with Zymenol and Zymelose

Gentle, non-irritating action of Zymenol accounts for its unusual effectiveness in diverticulosis. Lubricating quality of sodium carboxymethylcellulose in Zymelose reduces possibility of impaction. For *safe* results, prescribe:

Zymenol . . . the emulsion containing brewers yeast

- Non-habit forming
- No leakage
- No irritants
- Sugar free

Zymelose . . . the handy tablets and tasty granules containing SCMC and debittered brewer's dried yeast fortified with Vitamin B-1

- Bulk without bloating
- Mild, gentle
- Effective

EFFECTIVE BOWEL MANAGEMENT

CLIP AND MAIL THIS COUPON

OTIS E. GLIDDEN & CO., INC.
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PLEASE SEND SAMPLES
☐ *Zymenol* EMULSION
☐ *Zymelose* TABLETS
☐ *Zymelose* GRANULES

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THE RECONSTRUCTIVE IRON TONIC.....

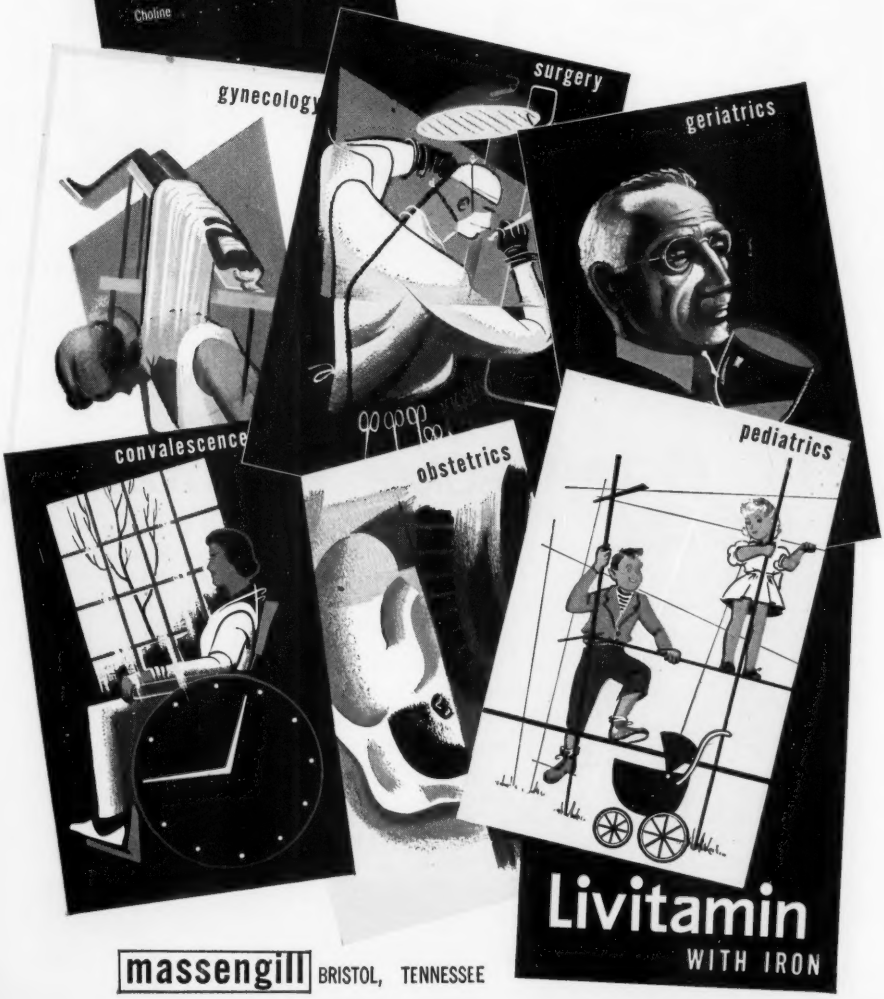
of wide application

Each fluidounce represents:	
Iron Peptonized (Equiv. in elemental iron to 70 mg.)	420 mg.
Manganese Citrate, Soluble	158 mg.
Thiamine Hydrochloride	10 mg.
Riboflavin	10 mg.
Vitamin B_{12} (Crystalline)	20 mcg.
Niacinamide	50 mg.
Pyridoxine Hydrochloride	1 mg.
Pantothenic Acid	5 mg.
Liver Fraction 1	2 Gm.
Rice Bran Extract	1 Gm.
Inositol	30 mg.
Choline	60 mg.

Provides the multiple requirements for effective treatment of nonspecific asthenia.

The combined therapy is designed to increase appetite and improve the blood picture. Better digestion and improved anabolism are part of the corrective process.

Livitamin is designed to treat the entire syndrome



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Especially for Elderly Patients . . . in

CHRONIC URINARY INFECTIONS

Better Control with Less Control . . .

★*Non-Toxic*
★*No Drug Fastness*
★*May Be Given Over Long Periods of Time*

A self-acidifying methenamine urinary antiseptic permitting high dosage without toxicity. Quickly soothes inflamed mucosa. Bacteriostatic against E. Coli, S. Albus, S. Aureus. Requires no periodic blood tests, etc. May be prescribed alone or with suitable antispasmodics and sedatives as individually required—tr. belladonna, tr. hyoscyamus, phenobarbital, etc. Especially useful for older patients.

(Sample Prescription)

℞ Tr. Belladonna ʒii
Urolithia gs. ad. ʒviii
Sig ʒii 2 p.d.c. cup
warm water ½ hr. AC.

UROLITHIA

SEND FOR SAMPLES

Cobbe Phar. Div.— BORCHERDT MALT EXTRACT CO.
217 N. WOLCOTT AVE. :: CHICAGO 12, ILLINOIS

For the Aged and Senile Patient

ORAL *Metrazol*

— to help the geriatric patient with early or advanced signs of mental confusion attain a more optimistic outlook on life, to be more cooperative and alert, often with improvement in appetite and sleep pattern.
Metrazol, a centrally acting stimulant, increases respiratory and circulatory efficiency without over-excitation or hypertensive effect.

Dose: 1½ to 3 grains, 1 or 2 teaspoonfuls Liquidum, or the tablets, every three or four hours.

Metrazol tablets, 1½ grs. (100 mg.) each. Metrazol Liquidum, a wine-like flavored 15 per cent alcoholic elixir containing 100 mg. Metrazol and 1 mg. thiamine HCl per teaspoonful.

Metrazol®, brand of pentylenetetrazol, a product of E. Bilhuber, Inc.

BILHUBER-KNOLL CORP. *distributor* **ORANGE NEW JERSEY**

A *Leeming* First:

the **New** *coronary vasodilator*

Metamine®

Leeming brand of triethanolamine trinitrate biphosphate

more effective in angina prevention

than other coronary dilators. When taken routinely, METAMINE prevents anginal attacks or greatly diminishes their number and severity. In addition, METAMINE is apparently nontoxic, even in prolonged or excessive dosage.

there is a reason

METAMINE is chemically distinct from all other organic nitrates in that it has a nitrogen, rather than a carbon linkage. This perhaps explains its greater effectiveness and freedom from side effects.

Dosage: METAMINE is effective in a dosage of **only 2 mg.** To prevent anginal attacks, swallow 1 METAMINE tablet after each meal, and 1 or 2 tablets at bedtime. Full preventive effect is usually attained after third day of treatment.

Supplied: METAMINE tablets, **2 mg.**, vials of 50.

Thos. Leeming & Co. Inc. 155 EAST 44TH STREET, NEW YORK 17, N.Y.

Doctors . . .

For recommendation to your patients over 60, the Cold Spring Project is a pilot experiment in residential adult education for college graduates, men and women of good physical and mental health. For a period of six or nine months, the residents engage in an active program in the creative arts—painting, ceramics, writing; such crafts as woodworking, photography; and a program of lectures and discussions led by men and women prominent in their special fields of the humanities, the sciences and social problems. The entire program is organized around the individual needs of the registrants who are urged but not required to participate in a wide variety of activities. Medical, psychiatric and psychological consultation and counselling available to registrants as desired.

For information brochure, write:

RUTH ANDRUS, Ph. D., *Director*
The Cold Spring Project
COLD SPRING-ON-HUDSON 7,
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reinforced action
in common infections

Erythro-sulfa*

antibiotic action of erythromycin
chemotherapeutic
effect of triple sulfonamides

valuable especially in staphylococcal, streptococcal, and pneumococcal infections

Each tablet contains

Erythromycin . . . 100 mg.
Sulfadiazine . . . 0.083 Gm.
Sulfamerazine . . 0.083 Gm.
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THE UPJOHN COMPANY, KALAMAZOO, MICHIGAN

Old Age Benefits . . .
from TESTRAMONE *and* VITRAMONE

Testramone and Vitramone have an important place in the treatment of general debilities of old age, such as poor appetite, bad sleeping habits, inadequate nutrition, hepatic insufficiency, bowel impairment and dysfunction, tired sluggish feeling, and similar conditions. Supplied in 10 cc. multiple dose ampul vials for intramuscular injection. Recommended dose 1 cc., most effective when ½ cc. each is given in same syringe.

FORMULAE

TESTRAMONE*— Each CC. Contains:

Testosterone in macrosuspension	12½ mg
Thiamine HCl	10 mg
Riboflavin	2 mg
Pyridoxine HCl	5 mg
Niacinamide	40 mg
Inositol	50 mg
Choline Chloride	10 mg
d.l. Methionine	10 mg
Benzyl Alcohol	1%
Chlorobutanol (chloral derivative)	½%
Distilled water q.s.	1 cc.

VITRAMONE*— Each CC. Contains:

Natural estrogenic hormone in macrosuspension	1 mg or 10,000 Intern units
Thiamine HCl	10 mg
Riboflavin	2 mg
Pyridoxine HCl	5 mg
Niacinamide	40 mg
Inositol	50 mg
Choline Chloride	10 mg
d.l. Methionine	10 mg
Benzyl Alcohol	1%
Chlorobutanol (chloral derivative)	½%
Distilled water q.s.	1 cc.

*U. S. Patent applied for.

Send for literature and professional samples of these aids in the treatment of male climacteric and menopause.

HARVEY Laboratories

5109 GERMANTOWN AVENUE
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When diet restriction limits nutrition

Vitamins alone are not always enough

Based on the well recognized concept of interrelationship in nutrition, "Clusivol" Capsules offer an extensive formulation of vitamins, minerals, and trace elements . . . factors likely to be lacking when restrictive diets are prescribed.

REDUCING DIETS
DIABETIC DIETS
GERIATRIC DIETS
POSTOPERATIVE DIETS
PEPTIC ULCER DIETS
LOW SODIUM DIETS
HEPATIC DISEASE DIETS
RHEUMATIC FEVER DIETS

2 "Clusivol" Capsules (average daily dosage) provide:

Vitamin A (synthetic)	25,000 U.S.P. Units
Vitamin D (irradiated ergosterol)	2,000 U.S.P. Units
Vitamin C (ascorbic acid)	150.0 mg.
Thiamine HCl (B_1)	10.0 mg.
Riboflavin (B_2)	5.0 mg.
Pyridoxine HCl (B_6)	1.0 mg.
Panthenol, equivalent to ... of calcium pantothenate	10.0 mg.
Vitamin B_{12} U.S.P. (crystalline)	2.0 mcg.
Folic acid	2.0 mg.
Nicotinamide	100.0 mg.
Vitamin E (as mixed tocopherols natural)	10.0 mg.
Inositol	30.0 mg.
Choline—from choline bitartrate	30.0 mg.
Biotin	0.1 mg.
d-Methionine	20.0 mg.
Cobalt—from cobalt sulfate	0.1 mg.
Copper—from copper sulfate	1.0 mg.
Fluorine—from calcium fluoride	0.025 mg.
Iron—from 4 gr. ferrous sulfate exsic.	76.2 mg.
Calcium—from dicalcium phosphate	165.0 mg.
Manganese—from manganous sulfate	1.0 mg.
Iodine—from potassium iodide	0.15 mg.
Molybdenum—from sodium molybdate	0.2 mg.
Potassium—from potassium sulfate	5.0 mg.
Zinc—from zinc sulfate	1.2 mg.
Magnesium—from magnesium sulfate	6.0 mg.
Phosphorus—from dicalcium phosphate	127.4 mg.

"CLUSIVOL"® CAPSULES

Multiple vitamin-mineral supplement

No. 293—Supplied in bottles of 100 and 1,000.

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New York, N. Y. • Montreal, Canada

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5327

WYETH PRODUCTS IN CLINICAL APPLICATION

WYCHOL® in the correction of abnormal patterns of fat metabolism.

Clinicians frequently observe noteworthy subjective improvement in patients receiving lipotropic medication for various conditions.[1,2] Empiric findings of this nature are abundantly supplemented by clinical and experimental observations indicating that: *Lipotropic substances can and do influence favorably certain abnormal patterns of lipid turnover.*

Confirmation of the value of lipotropic therapy in fatty infiltration of the liver is afforded by numerous published reports. These are perhaps best summarized by Pollak's observation that

> "The reversal of hepatic steatosis and the improvement of the patients' well-being justify fully the usage of lipotropics . . ."[3]

Effect In Atherosclerosis

A number of clinicians have reported that lipotropic factors aid in the reduction of hypercholesteremia,[4] and that their daily use favorably influences the mortality rate in coronary atherosclerosis.[5]

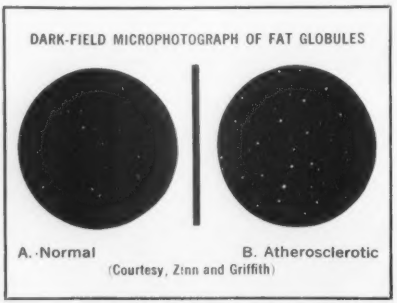
During the past few years, a great deal of experimental and clinical investigation has been directed to studies on etiologic factors in atherosclerosis. An important contributory factor is a high relative concentration of chylomicrons—fat particles 0.3 micron in diameter or larger—in the circulating blood of the fasting patient.[6,7] Recently, Labecki[8] has shown that a nutritional lipotropic regimen continued over a period of several months influenced the ratio of these lipids profoundly "in the direction of apparent normality."

Lipotropic therapy lowers the chylomicron level.[8]

A potent lipotropic combination—Syrup WYCHOL, choline and inositol, Wyeth—provides in each tablespoonful (15 cc.), 3 Gm. *choline base* (equivalent to 7.5 Gm. choline dihydrogen citrate) *plus* 0.45 Gm. inositol. WYCHOL is pleasantly flavored to encourage patient acceptance. Dosage with WYCHOL may be conveniently adjusted to suit the individual case.

WYCHOL is supplied in bottles of 1 pint and is also available as Capsules WYCHOL in bottles of 100 and 1000.

A new Syrup WYCHOL B is now available for your use. It contains WYCHOL to which has been added vitamin B_1, 2.5 mg.; vitamin B_2, 0.5 mg.; vitamin B_6, 2.5 mg., and niacinamide, 10 mg., in each 3 teaspoonfuls (15 cc.).



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Haven for the Hypertensive

Conservative living – avoiding unnecessary emotional as well as physical stress, providing real relaxation – and conservative medication are essential parts of the effective management of arterial hypertension.

Theominal – time-tested vasodilator and sedative – is helpful to many thousands of hypertensives. Continuous administration of Theominal often holds the blood pressure at a nearly normal level, relieving the congestive headache, chest pains and vertigo which frequently accompany hypertension.

WINTHROP

THEOMINAL®

(Theobromine 5 grains, Luminal ½ grain)

Vasodilator and Sedative for

ARTERIAL HYPERTENSION

•

When less sedation is required:

new THEOMINAL (M)

(Theobromine 5 grains, Luminal ¼ grain)

WINTHROP-STEARNS INC.

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Theominal and Luminal (brand of phenobarbital), trademarks reg. U.S. & Canada

CLINICAL EVALUATION FREQUENTLY FAVORS

BUTAZOLIDIN®

(brand of phenylbutazone)

In antiarthritic potency, BUTAZOLIDIN can be compared only with gold, ACTH and cortisone. In making a choice between these agents, the specific advantages of BUTAZOLIDIN merit consideration:

- Simple oral administration
- Potent and prompt antiarthritic effect
- Broad spectrum of action embracing many forms of arthritis
- No development of tolerance requiring progressively increasing dosage
- No disturbance of normal hormonal balance
- Moderate in cost

As with any agent so potent as BUTAZOLIDIN, optimal therapeutic results with minimal risk of side reactions can only be obtained by clinical management based on careful selection of patients, proper regulation of dosage, and regular observation of each patient.

Detailed Literature on Request.

BUTAZOLIDIN® (brand of phenylbutazone) Tablets of 100 mg.

GEIGY PHARMACEUTICALS

Geigy

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